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STUDIES IN TUBERCULOSIS.

By REGINALD WEBSTER, M.D., D.Sc., F.R.A.C.P.,
Pathologist to the Children's Hospital, Melbourne.

III. SYMPTOMLESS TUBERCULOUS BACILLURIA AS OBSERVED IN SUBJECTS OF OSSEOUS AND PULMONARY TUBERCULOSIS.¹

In the casting of a net for the collection of pathological material likely to provide cultures of *Mycobacterium tuberculosis* which might be examined with a view to the differentiation of human and bovine types, it was so disposed as to include within its meshes a series of specimens of urine from patients affected with tuberculosis of bones and joints as one group, and from patients with pulmonary tuberculosis as another. The findings which I now wish to present concerning the incidence of tuberculous bacilluria in the clinical states indicated are of the nature of gleanings in the field of the major inquiry rather than the results of a direct attack upon the problem of tuberculous bacilluria, its prevalence and significance.

Hæmatogenous Infection.

I venture to think that I am right in suggesting that to the majority of practitioners and students of medicine the term "disseminated tuberculosis" conveys only one meaning and conjures up a picture of severe and generalized miliary tuberculosis. Actually, dissemination of bacilli is a frequent occurrence in tuberculous patients, and miliary tuberculosis but its extreme clinical form. Tuberculous infection is to be regarded as a metastasizing process, and circulatory dispersion of bacilli is recognized as happening commonly in patients in whom active focal

tuberculous lesions are established. The conception of intermittent and not infrequent seeding of bacilli from an active tuberculous focus is simple and rational, and explanatory of the clinical phenomena of tuberculosis to a degree which has gained its general acceptance. It is probably not so commonly appreciated that experimental evidence by no means to be ignored exists in support of the contention that a measure of circulatory distribution of tubercle bacilli occurs at the time of primary infection. Careful study of tuberculosis induced in guinea-pigs by subcutaneous inoculation has resulted in observations which indicate that, in addition to the orderly step-like progression of infection from the inoculation focus to the immediately related lymph glands, thence to the next proximal group of glands, and so on, there is an almost immediate carriage of some bacilli to points at a distance from the place of entry, and if the infecting microorganisms are numerous, to diverse destinations in widely separated tissues.

In a notable address on the spread of tuberculous infection in the body, A. K. Krause² indicated the experimental evidence on which these statements are based. Krause studied systematically the manner and rate of distribution of living virulent tubercle bacilli in the bodies of guinea-pigs which had received a single subcutaneous inoculation. He found that dispersion of bacilli was amazingly rapid; long before the local granuloma became evident, living bacilli were recoverable from almost any of the animal's tissues. By the inoculation of various tissues into other guinea-pigs it was proved that tubercle bacilli had traversed the body and located themselves in many organs within four days or less. Such fixation took place weeks before visible changes appeared in the distant organs. Further observations on the part of A. K. Krause and his associate, H. S. Willis, relative to the rate of mobilization of living tubercle bacilli within the first few days after their inoculation into guinea-pigs, will be found in the address² to which I have referred.

¹ A report to the National Health and Medical Research Council of Australia.

In the development of their thesis that tuberculous meningitis is not induced by direct hematogenous infection, as a phase of miliary tuberculosis, but arises independently of the terminal sowing from the rupture and discharge into the subarachnoid space of contiguous caseous foci, Rich and McCordock¹⁰ assign the origin of some of such local caseous foci to the dissemination of bacilli which they regard as a concomitant of primary infection.

Clinical evidence of the hemic broadcast of tubercle bacilli is provided by the frequency with which bone and joint tuberculosis and genito-urinary tuberculosis arise in persons who prior to the unlooked-for occurrence have never shown any manifestations of tuberculous disease. It cannot be reasonably contested that in such an event the bacilli responsible for the first clinically appreciable infection are carried to the affected organ or tissue by the blood stream from an unsuspected focus elsewhere in the subject. Nor is it likely, when quasi-primary kidney or bone tuberculosis does arise, that the bacilli initiating those lesions have been the only detachment to explore the bodily tissues by way of the blood stream. It must be allowed that an actual spreading of bacilli by the blood stream occurs much more frequently than the number of instances which come to clinical appreciation indicate. The foregoing principles have been epitomized by A. K. Krause in the dictum that there is no more certain fact in tuberculosis than that the number of infections of any structure is many times the number of symptomatic foci; this in turn may be reduced to the simple statement that clinical disease of an organ develops once for every five, ten or fifty times that bacilli lodge there.

If it be conceded that more or less frequent "seeding" of bacilli from an active tuberculous focus occurs, with concomitant low-grade, probably intermittent and evanescent bacillæmia, then the kidney is exposed along with other organs, and is a favourable viscus in which to study symptomless infection, because of the possibility of detection of tubercle bacilli in the urine.

The frequency of tuberculous infection of the kidney, as distinguished from clinically evident renal tuberculosis, has been underestimated in the past. There is no doubt that in association with other active hematogenous lesions, such as those of bones and joints, renal tuberculosis is not uncommon. In the early stages, which may persist for some years, there are no urinary symptoms whatever; pyuria is often very slight and apt to be intermittent, so that it will be overlooked unless careful and repeated examinations of the urine are made.

Results of Investigation.

During the year 1938 and the succeeding two years I recovered *Mycobacterium tuberculosis* from 134 specimens of urine derived from 122 patients. All the strains were secured by direct cultivation, with the exception of six for which the tissues of a guinea-pig inoculated with appropriately prepared urinary deposit were employed. On the basis of their dominating clinical features, the patients from whom urinary cultures of *Mycobacterium tuberculosis* were obtained may be grouped as follows:

(i) Genito-urinary tuberculosis	54
(ii) Osseous tuberculosis	38
(iii) Pulmonary tuberculosis	30

The cultural results obtained in confirmation of the clinical diagnosis of genito-urinary tuberculosis have no place in the present discussion, which is concerned with the frequent occurrence of symptomless tuberculous bacilluria in subjects of osseous and pulmonary tuberculosis and the manner in which such bacilluria may be demonstrated.

Osseous Tuberculosis.

Specimens of urine were collected from 82 patients suffering from tuberculous disease of bones and joints; of these, 18 were children, inmates of the Children's Hospital orthopaedic section, Frankston, and 64 were adults. The majority of the adults, 56 in the total of 64, were patients of the Austin Hospital for Cancer and Chronic Diseases, Heidelberg, and for access to this source of essential material I am indebted to Dr. H. O. Johnston

and Dr. Medwin Hutson, both of whom held the office of medical superintendent of the Austin Hospital during the period of the research. The urinary specimens were collected with no regard to symptoms, it being sufficient that the patient was affected with bony tuberculosis.

While there is an obvious advantage in securing a large quantity of urine from an individual patient for the purpose of detecting tubercle bacilli, my experience in direct cultivation of *Mycobacterium tuberculosis* from urine leaves me more than doubtful of the utility of the time-honoured twenty-four hour specimen. Such round-the-clock collections are frequently offensive from ammoniacal fermentation and teeming with adventitious bacterial growth, which is reflected in an annoyingly high proportion of contaminated culture tubes. Unless the urine is collected in clean receptacles and refrigerated during the period of collection to arrest the multiplication of indigenous and acquired bacteria, I prefer not to receive a twenty-four hour specimen. Twelve hours is quite a sufficient handicap to concede to contaminating micro-organisms, and for many months I have been requesting that the specimen be secured by conservation of the urine which the patient passes on retiring for the night and adding to this amount the first specimen passed in the morning. The necessity for prompt transmission to the laboratory is of course duly emphasized.

From the urine of no less than 32 of 64 adult patients whose conspicuous clinical disease was tuberculosis of one or more bones and joints, acid-fast and alcohol-fast bacilli were cultivated, exhibiting the cultural characters of the human type of *Mycobacterium tuberculosis*. This high proportion of "positive" findings (50%) was registered in the main by a single cultural test, as for only four of the 32 patients shown to exhibit tuberculous bacilluria were other measures employed. Two were patients of the Alfred Hospital, in the investigation of whom Dr. R. A. Willis had inoculated guinea-pigs with the urinary deposits and kindly forwarded me the resulting tuberculous tissues from the animals; the other two were Austin Hospital patients, a repetition of the cultural examination of whose urine succeeded in demonstrating the presence of tubercle bacilli after failure at the first attempt.

Of the 32 subjects of tuberculous disease of bone thus shown to be discharging tubercle bacilli in the urine, 10 only made complaint of symptoms such as would draw attention to the urinary tract. Twenty-two of these patients therefore exemplified that state of symptomless tuberculous bacilluria from which has sprung what I firmly believe to be the erroneous conception of "excretory bacilluria". It is a noteworthy and significant point that in 18 of these 22 instances of symptomless tuberculous bacilluria arising in the course of osseous tuberculosis, the findings by microscopic examination of the urine furnished evidence of an established lesion in the form of red blood cells, excess of leucocytes, or both.

Cultural investigation of the urine of 18 children affected by tuberculosis of bone resulted in the recovery of *Mycobacterium tuberculosis* from this source in six instances; as all six patients displayed clinical signs and symptoms indicative of involvement of the urinary system, this small series provided no instance of symptomless tuberculous bacilluria. The findings relating to the incidence of tuberculous bacilluria in subjects of bone and joint tuberculosis are assembled in Table I.

TABLE I.
Tuberculous Bacilluria as Observed in Osseous Tuberculosis.

Subjects.	Number.	Positive Results.	Percentage of Positive Results.
Children	18	6 ¹	33.3
Adults	64	32 ²	50.0
Totals	82	38	46.4

¹ Signs and symptoms present in all.

² Signs and symptoms present in 10, no symptoms in 22; but of these 22 18 provided microscopic signs and four provided no signs.

The finding, with few exceptions, by a single cultural test that 32 (50%) of 64 adult patients suffering from bone and joint tuberculosis were discharging tubercle bacilli in the urine, at first sight compares more than favourably with results obtained by R. I. Harris,²⁰ of Toronto, in a similar investigation based upon repeated guinea-pig inoculations for the detection of *Mycobacterium tuberculosis* in the urine. Harris reported having demonstrated the existence of tuberculous bacilluria in 16 (37%) of 43 adult subjects of bone and joint tuberculosis, nine of whom exhibited no symptoms to suggest a renal complication. He proceeded by the inoculation of guinea-pigs with urinary deposit from each patient at intervals of two months, thus securing for most of them a long series of bacteriological examinations of the urine. Some of the adults were observed over a period of five years, and the majority for between two and three years; the minimum period of investigation was eighteen months. As has already been stated, 16 of 43 patients excreted tubercle bacilli in the urine, either intermittently or constantly; nine of the 16 displayed no symptoms suggestive of any urinary disorder.

In my examination of 64 adult sufferers from bone and joint tuberculosis, cultures from the urine were made on four occasions for one subject, three times for three persons, and twice for eight others. For the remaining 52 patients only one bacteriological examination directed towards the detection of *Mycobacterium tuberculosis* was made, by culture in 50 instances and by guinea-pig inoculation in two. By comparison with the carefully planned attack on the question at issue conducted by Harris, these procedures seem inadequate and perfunctory, as indeed they would have been had observations on the incidence of tuberculous bacilluria in subjects of bone and joint tuberculosis been the primary object of the investigation. In spite of less searching inquiry, however, my figure for positive findings by direct cultivation—50% of 64 individuals—was higher than that of Harris by guinea-pig inoculation—37% of 43 patients.

For one who has already advocated direct cultivation as preferable to guinea-pig inoculation in routine work for the detection of *Mycobacterium tuberculosis*, there is an obvious opportunity to claim the foregoing comparison of results as evidence in support of the contention. Such a claim, however, would be open to the criticism that factors other than bacteriological technique have also to be considered, and it is therefore not advanced. Patients received at the Austin Hospital for Cancer and Chronic Diseases are with few exceptions in an advanced stage of their malady, and it is probable that a group of subjects of bone and joint tuberculosis from such an institution would exhibit a maximum amount of systemic tuberculosis. I would submit this consideration as the probable explanation of the high incidence of tuberculous bacilluria disclosed by a survey which was admittedly not exhaustive.

At the Hospital for Sick Children, Toronto, R. I. Harris²¹ also demonstrated tubercle bacilli in the urine of nine among 67 children (13.8%) affected with bone and joint tuberculosis. Eight of the nine children presented no symptoms referable to the kidneys or urinary tract, the only clinical sign that all was not right in the urinary system being a mild degree of pyuria, recognizable only by microscopic examination. The existing state of affairs was disclosed by the routine injection of urinary deposit into guinea-pigs every two months over a period of eighteen months. Prior to the institution of these measures tubercle bacilli had been detected in the urine of only one among 392 patients.

Pulmonary Tuberculosis.

In the endeavour to assemble cultures of *Mycobacterium tuberculosis* from as many sources as possible other than specimens of sputum, I sought the cooperation of Dr. D. B. Rosenthal, medical superintendent of the Gresswell Sanatorium, Mont Park, Victoria. Dr. Rosenthal kindly arranged the regular transmission of six specimens of urine per week, collected from male subjects of pulmonary tuberculosis, irrespective of the presence or absence of symptoms of urinary disorder. In this manner specimens

of the urine of 79 patients were secured for cultural examination by methods appropriate to the growth of *Mycobacterium tuberculosis*. To these are to be added specimens of urine from 38 other adults of both sexes suffering from pulmonary tuberculosis; the majority were from patients of the Austin Hospital, but a few from private sources are included.

Of 117 adult subjects of pulmonary tuberculosis, 30, or 25.6%, exhibited tuberculous bacilluria, as determined with five exceptions by a single cultural test. Symptoms indicative of renal, or more correctly, vesical infection were present in 11 only, so that of the 30 persons for whom a positive bacteriological finding was obtained, 19 exhibited the state of symptomless tuberculous bacilluria.

The situation as regards the occurrence in pulmonary tuberculosis of tuberculous bacilluria with no revealing symptoms is best examined in the data relating to the patients from the Gresswell Sanatorium, as for the purpose I have the advantage of a careful analysis of the essential facts concerning each patient, kindly supplied to me by Dr. Winston Smith.

In the Gresswell group of 79 men, all affected with active pulmonary disease and with few exceptions discharging tubercle bacilli in the sputum in numbers sufficient to render them detectable by the microscopic search of smear preparations, *Mycobacterium tuberculosis* was cultivated from the urine of 18, a proportion of positive findings of 22.7%. Thirteen of the successful cultivations were registered from the first specimen of urine examined, and the remaining five were secured at a second attempt. Fourteen of the 18 men in whom tubercle bacilli were shown to be present in the urine offered no symptomatic suggestion of the fact; in four men symptoms were present and supported by signs in the form of red blood cells, pus cells, or both, as determined by microscopic examination of the urine; in six, although there were no symptoms, microscopic signs were not wanting, and in eight absence of symptoms was paralleled by an apparent dearth of signs in the several specimens of urine from each patient submitted to microscopic examination.

Six of the eighteen Gresswell patients from whom a urinary culture of *Mycobacterium tuberculosis* was obtained subsequently died, and post-mortem examination was secured in five instances. Renal tuberculosis, macroscopically evident, was proved in two, while in the kidneys of the other three subjects the tuberculous infection probably existent was not apparent on macroscopic inspection.

The observations relating to the incidence of tuberculous bacilluria in 117 subjects of pulmonary tuberculosis are summarized in Table II.

TABLE II.
Tuberculous Bacilluria as Observed in Pulmonary Tuberculosis.

Source of Material.	Number of Patients.	Number Exhibiting Tuberculous Bacilluria.	Percentage of Positive Results.
Gresswell group	79	Symptoms present 4 Symptoms absent 14 } 18	22.7
Austin Hospital and private sources.	38	Symptoms present 7 Symptoms absent 5 } 12	31.6
Totals ..	117	Symptoms present 11 Symptoms absent 19 } 30	25.6

It has been stated^{22,23} that tuberculous bacilluria occurs more frequently in patients affected with osseous tuberculosis than in those with "only pulmonary tuberculosis" (Harris). I am prepared to accept the statement, but not the reasoning on which it is based. The appearance of tuberculous disease in bone is held by Harris to indicate that the blood stream has already been invaded, whereas in pulmonary tuberculosis the disease is still limited to the site of infection. Tuberculosis is a systemic disease, even as syphilis, and a greater liability to renal metastatic

foci in the presence of bony lesions is better to be explained on the ground that the invading bacilli, already possessed of a concealed bridgehead by which they enter the blood stream, have succeeded in establishing a forward base in a site particularly favourable for their further access to the circulation.

It is probable that the incidence of tuberculous bacilluria in pulmonary tuberculosis is lower than in tuberculous disease of bone, but it is surely higher than would be deduced from the results obtained by Menton.⁴⁰ In a paper dealing with "excretory bacilluria" in relation to the diagnosis of renal tuberculosis, Menton reported having inoculated guinea-pigs with the urinary deposits from 76 patients in the sputum of all of whom tubercle bacilli were to be found by direct microscopic search. In none of the subjects of the investigation were there any symptoms of genito-urinary involvement, nor was chemical or microscopic abnormality detected in their urine. In only one of the 76 subjects of pulmonary tuberculosis was a positive finding obtained with respect to the presence of tubercle bacilli in the urine. One specimen of urine only from each patient was examined bacteriologically. In later work⁴¹ Menton carried out repeated animal inoculation tests with specimens of urine from a smaller number of patients affected with pulmonary tuberculosis. One hundred samples of urine were collected from 22 patients and the deposits were inoculated into guinea-pigs, with the result that only one specimen was thereby shown to contain tubercle bacilli.

Contrasting with the results obtained by Menton, are those of W. S. Mack,⁴² as reported in a short paper entitled "Excretory Bacilluria" and published in the *Edinburgh Medical Journal*. Mack carried out examinations of the urine of 21 tuberculous patients, whose clinical manifestations were extra-urinary and in the main pulmonary. Twenty-four hour specimens of urine were collected at intervals of one week, and repeated bacteriological examinations were undertaken for each subject. One patient developed frank renal tuberculosis; but of the other 20 no less than 15 exhibited tuberculous bacilluria by guinea-pig inoculation tests; the intermittent discharge of tubercle bacilli was indicated by the fact that in none of the patients were the microorganisms in question demonstrated in every specimen of urine examined. Urine from one patient in the group was on 14 occasions submitted to the animal inoculation test, with results consisting of ten "negative" and four "positive" findings. None of the 20 patients displayed any symptoms referable to the urinary system or developed clinical indications of renal tuberculosis for as long as it was possible to observe them. Brevity ceases to be the soul of wit when, as in this terse communication, the author's interpretation of his findings is left to inference on the part of the reader. By implication it would seem that W. S. Mack's striking results are advanced in support of the theory of excretory bacilluria.

"Excretory Bacilluria."

It is scarcely possible to discuss the findings here recorded regarding the occurrence of symptomless tuberculous bacilluria without raking over the ashes of the burned-out controversy which has centred round the doctrine of "excretory bacilluria"—a term which implies that tubercle bacilli may be eliminated by kidneys which sustain no damage in the process. That tubercle bacilli may be discharged in the urine of patients who display no symptoms suggestive of the fact, is an observation of many years' standing, and the plausible explanation conveyed in the terms "excretory bacilluria" and "filtration bacilluria" was for a long time not seriously challenged. Many authorities, included among whom is Calmette, have propounded the teaching that tubercle bacilli may be excreted by healthy kidneys, and the seal of text-book approval has been placed upon it by Thomson-Walker.⁴³ But no matter what the stature of the giants of the past who have sponsored this conception, or the standing of the text-books which have endorsed it, the theory of excretory bacilluria can no longer withstand the weight of evidence against it.

In the first place it seems improbable that the kidney can excrete tubercle bacilli with any greater facility than it can eliminate any other form of particulate matter. The experimental work of Helmholtz and his associates,^{44,45} in which they employed a variety of microorganisms but no tubercle bacilli, demonstrated that the kidney did not excrete bacteria in the usual sense of the term; and that microorganisms did not appear in the urine in the absence of focal lesions in the kidneys. In experimental work on non-tuberculous bacteriuria, those investigators who have included careful histological study of the kidneys in their observations, have always found that pathological changes, such as blood vessel rupture, severe epithelial degeneration, or glomerulonephritis, developed before the "excretion" of microorganisms occurred.

Experimental data specifically relating to the possibility of the excretion of tubercle bacilli by the kidneys have been supplied by Lieberthal and von Huth.⁴⁶ The workers named introduced tubercle bacilli in very large numbers into the circulation of rabbits, and by placing the animals in metabolism cages were enabled to collect the total urine voided for periods up to twenty days. The whole of each twenty-four hour collection was centrifuged and daily cultures were prepared by the Löwenstein technique on the egg medium of Hohn. In eight animals tubercle bacilli were injected into the ear vein, and in six suspensions of *Mycobacterium tuberculosis* were introduced into the circulation by intracardiac injection. Tubercle bacilli could not be demonstrated in the urine of any animal by microscopic and cultural examination of the total urine excreted for a period of twenty days, and this notwithstanding the fact that tuberculous lesions developed in the kidneys of three of the rabbits within the period of the experiments. In eight other animals a degree of nephritis, evidenced by the presence of albumin, red blood cells and casts in the urine, was induced by the injection of solutions of mercuric chloride and uranium nitrate or of cantharidin in oil, prior to the intravascular injection of tubercle bacilli; but the renal damage so occasioned did not render the kidneys any more permeable to tubercle bacilli.

Of the many laboratory studies directed towards determining the significance of symptomless tuberculous bacilluria, those of E. M. Medlar are the most exhaustive and convincing. With K. T. Sasano,⁴⁷ Medlar instituted an inquiry based on careful examination of the urine combined with histological study of the kidneys. Guinea-pigs inoculated subcutaneously with human tubercle bacilli and rabbits injected intravenously with bacilli of bovine type were placed in metabolism cages and the total urinary output was collected from each animal, in twenty-four hour quantities or greater, over a period of several days or weeks. The deposit from each specimen of urine was examined for the presence of pus cells and tubercle bacilli and inoculated into a normal guinea-pig. Negative findings attended the examination of the urine collected from all the rabbits. In five guinea-pigs tubercle bacilli were shown to be present in the urine by the inoculation of other healthy guinea-pigs. Serial sections of the kidneys of every animal of which the urine had been examined were prepared, regardless of the gross appearance of the organs. It was thus determined that tuberculous lesions were present in the kidneys of all the animals exhibiting tuberculous bacilluria, that the size of the tuberculous lesions was no criterion as to the number of bacilli discharged from it, and that negative findings in the urine did not exclude the possibility of tuberculous infection of the kidneys. Medlar and Sasano were insistent that serial sections were essential if the danger of overlooking tuberculous lesions in the kidneys were to be avoided.

In a later study⁴⁸ Medlar showed that of 30 patients who died of pulmonary tuberculosis, 22 had renal lesions, although none had displayed urinary symptoms before death. This particular research was designed and executed on an heroic scale, involving as it did the preparation and examination of 100,000 serial microscopic sections of the kidneys to be investigated. The lesions were all small, often microscopic in size; in every instance they were bilateral, and—a very important observation—many

showed indubitable evidence of healing. The pathological processes noted in the organs represented lesions of different age and severity, suggesting that the kidneys had been called upon to withstand recurring blood-borne showers of tubercle bacilli, some of which had effected a lodgement and initiated tuberculous infection. In this study no observations were made on the presence of tubercle bacilli in the urine of the patients; but Medlar judged from the appearance of inflammatory exudate and tubercle bacilli in the lumina of tubules that six of the 30 patients should have exhibited tuberculous bacilluria.

Another worker in the same field is David Band,⁶⁰ whose report was published in 1935. Band investigated for tuberculous bacilluria 174 cases of extra-urinary tuberculosis. Symptoms were absent from all; cystoscopic and pyelographic evidence of urinary tuberculosis was also lacking. From 25, or 14.4%, of the subjects in the group tubercle bacilli were recovered from the urine by the animal inoculation test. It is to be noted that pus cells were present in excess in every specimen of urine yielding a positive finding. The kidneys of five patients in whom tuberculous bacilluria had been present were secured at necropsy. No macroscopic evidence of tuberculous infection was found, but on microscopic examination of serial sections—no less than 1,500 to 2,000 from each half kidney—renal lesions were found in each of the five patients.

The industry and tenacity of such workers as Medlar and Band compel admiration; their results carry conviction and render the theory of "excretory bacilluria" untenable.

The presence of tubercle bacilli in the urine implies tuberculous infection of the kidneys as a necessity. The lesions induced are often of microscopic dimensions, possibly no more than minute interstitial foci which make communication with adjoining tubules, or ulcerative processes involving glomeruli; they excite no symptoms and lie beyond the range of clinical perception. Such clinically silent renal tuberculous damage arises commonly in subjects of osseous tuberculosis and less frequently in patients in whom tuberculous disease presents itself as pulmonary tuberculosis. Fortunately many such minimal lesions heal and only a minority progress to the destruction and cavitation—renal phthisis—which demand nephrectomy.

Conclusion.

The observations which provoked the foregoing discussion were gathered by the way in the course of intensive work in the cultivation of *Mycobacterium tuberculosis*⁶¹ and the differentiation of human and bovine types.⁶² Incidental as they are, not the result of an investigation directed specifically towards ascertaining the frequency of occurrence of symptomless tuberculous bacilluria in bone and joint and pulmonary tuberculosis, the findings are sufficiently significant to warrant their presentation in this manner. In view of the fact that in persons affected with extra-urinary foci of active tuberculous disease tuberculous bacilluria occurs intermittently, is here today and gone tomorrow, it is obvious that results based mainly upon a single cultural test of the urine must underestimate the true position. Even so, it was found that in one group of 64 adult subjects of bone and joint tuberculosis 32 (50%) were discharging tubercle bacilli in the urine; in another group of patients whose illness manifested itself clinically as pulmonary tuberculosis, 30 (25.6%) of 117 exhibited tuberculous bacilluria. In both groups the majority of subjects from whose urine *Mycobacterium tuberculosis* was cultivated displayed no symptoms of urinary disorder.

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THE VALUE OF IMMUNIZATION IN PERTUSSIS.¹

By DONALD VICKERY, M.B., Ch.M., M.R.A.C.P.,
Sydney.

THE subject of pertussis immunization has so often been dealt with in the medical literature in recent years that it seems almost unnecessary to bring it again before the notice of the medical profession; but here in New South Wales we have recently come through another whooping cough epidemic, with its usual high mortality rate amongst little children, so that further investigation of the subject of immunization seems eminently justifiable.

During the last ten years in Australia there have been many doubts amongst medical men as to the efficiency of pertussis vaccine as a prophylactic against whooping cough, and rightly so. These doubts have been more pronounced in this country because it has only been in recent years that we have realized the importance of Leslie and Gardner's work² on the phases of *Haemophilus pertussis*, and have learned that vaccine, unless made from the Phase I growth of the organism and prepared according to special technique, is useless from the standpoint of conferring immunity in this disease.

In 1929, when I was in charge of the pertussis clinic at the Royal Alexandra Hospital for Children, I became convinced of the efficiency of pertussis vaccine as a prophylactic agent. In an article in *THE MEDICAL JOURNAL OF AUSTRALIA* of November 14, 1931,³ I pointed out its great value, if administered to contacts prior to the onset of the earliest symptoms of coryza, and that in those cases in which it did not prevent the disease, the duration would be shorter and the disease milder. The vaccine used was that supplied by the Commonwealth Serum Laboratories and was administered in increasing doses every second or third day for four doses at least.

After the epidemic of 1934 I felt that the vaccine as supplied by the same makers was almost useless, and could explain the fact only on the grounds that the epidemic was caused by a different strain of organism. In the light of recent knowledge it is almost certain that the vaccine supplied in 1929 was "faked" from the Phase I growth of the organism.

The work of Leslie and Gardner, and the experiments carried out by numerous American workers and clinicians have now put vaccine Phase I prophylaxis beyond the experimental stage and established it as a most efficient controlling agent in this disease.

¹ Read at a meeting of the New South Wales Branch of the British Medical Association on June 26, 1941.

Before going further with this subject I should like to refer to certain aspects of the dangers and the epidemiology of whooping cough here in Sydney. First, what chances are there that our children will escape whooping cough if nothing is done for them? These can be assessed only from the figures of countries where pertussis is a notifiable disease. Stocks and Karn⁽¹⁾ (1932) showed that 44% of the children of London are attacked by the disease before five years of age. Collins⁽²⁾ found that in six places in five different States of the United States of America the percentage of persons who had had pertussis was within the limits 73% to 85%, and to illustrate the extreme contagion of the disease American writers have provided data on the proportion of children who develop whooping cough after contact with the disease. Schermerhorn,⁽³⁾ who assisted Dr. Pearl Kendrick in the Grand Rapids experiments, is one of the most conservative, and reports a rate of 75% in unvaccinated children in Grand Rapids, all being less than three years of age. He contrasts this with an attack rate of only 13.5% amongst vaccinated contacts. From this it can be seen that the number of cases of whooping cough in a community must be considerable and that a child's chances of missing the infection must be very remote indeed.

Secondly, what dangers do children run by contracting the disease? They risk (a) ill health and chronic lung damage and (b) death. The former we are unable to assess with any definite degree of accuracy. The amount of chronic ill health brought about by the prolonged course of pertussis is seen every day by those dealing with children. This ill health and lung damage pave the way for the direct establishment of chronic bronchitis, fibrosis, bronchiectasis and tuberculosis, and for the sensitizing of that reflex which is so often the cause of asthma in children. We have statistics to prove that here in New South Wales whooping cough has become the greatest killer of children aged under two years, with the exception of gastro-enteritis; and here I should like to refer to two statistical tables I published in THE MEDICAL JOURNAL OF AUSTRALIA in 1931.⁽⁴⁾ These tables show that in New South Wales 86% of the deaths from pertussis in the years mentioned occurred among children aged under two years and 63% occurred among children aged under one year. Meyers recently confirmed this fact by publishing statistics of New South Wales, extending from 1920 to 1938. His figures showed a death rate of 61.3% among children aged under one year. Also Dorothy Gepp⁽⁵⁾ (1940) stated that pertussis amongst all the infectious diseases was by far the most potent cause of infantile death. In New South Wales alone during the last fourteen years 1,718 children have died of pertussis, of whom 1,552, or 90%, have been under three years of age. Pertussis now is only narrowly outstripped by diphtheria and gastro-enteritis as the greatest cause of death amongst children of all ages.

Thirdly, I want to show you how pertussis has tended to attack the metropolis of Sydney in waves or epidemics

TABLE I.
Showing Death Rate from Pertussis for each of the First Five Years of Life, for all other Ages, and Total Death Rates.¹

Year.	Age Period (Years).						Total.
	1	1 to 2	2 to 3	3 to 4	4 to 5	Other Ages.	
1927 ..	142	36	12	10	3	8	211
1928 ..	63	31	2	2	3	2	103
1929 ..	128	52	15	9	2	6	212

¹ These tables show that 86% of the deaths from pertussis in the three years mentioned occurred in children aged under two years.

TABLE II.
Showing Number of Deaths from Pertussis among Children Under Two Years compared with Total Number of Deaths from Pertussis at all other Ages, and Percentage Under Two Years.

Year.	Number of Deaths of Children Aged Under Two Years.	Number of Deaths of Children at all Other Ages.	Total Deaths.	Percentage of Deaths of Children Aged Under Two Years.
1927 ..	178	33	211	84
1928 ..	94	9	103	91
1929 ..	180	32	212	85

in recent years, and how each epidemic has commenced almost at the same period of the year and has been limited to certain months of the year. This is seen in Table III. Each epidemic (there have been six in fourteen years) has commenced in July or August of each year, reached a crescendo in September, October, November and December, and rapidly died out in January and February, leaving March, April, May and June always free from the disease in epidemic proportions.

On no occasion has an epidemic come in two successive years. On one occasion there was a full two-year interval between epidemics, and prior to this last epidemic, beginning in August, 1940, there was a full three-year period of freedom from an epidemic. So we can reasonably suppose that if a child survives an epidemic in his first year of life he will be old enough by the next epidemic at least not to lose his life should he contract the disease. However, the child is still liable to be left with some crippling lung condition.

These three facts, (i) the extreme likelihood of infection, (ii) the high death rate among children aged under two years (approximately 85%), and (iii) the biennial or triennial epidemic nature of the disease, are of great practical importance when we consider protection by immunization and the best methods of applying it to gain maximum "life-saving" results.

The work of Sauer⁽⁶⁾ and of Charlotte Singer Brooks,⁽¹²⁾ Kendrick's⁽³⁾ Grand Rapids pertussis immunization study

TABLE III
Deaths from Pertussis: Metropolitan Area of Sydney, 1927 to 1940.

Year.	July.	August.	September.	October.	November.	December.	January.	February.	March.	April.	May.	June.	Total.
1927-28	4	6	20	14	11	11	6	3	1	2	—	—	78
1928-29	3	1	1	4	3	—	3	4	5	2	—	—	29
1929-30	3	10	18	20	39	28	18	7	2	3	4	2	152
1930-31	—	2	2	3	5	6	2	4	—	2	—	—	33
1931-32	6	9	22	32	15	17	9	6	1	—	—	1	118
1932-33	—	—	1	1	—	—	—	—	—	—	—	—	2
1933-34	—	—	3	—	1	4	8	7	6	6	5	8	46
1934-35	19	15	28	22	10	4	2	1	1	—	—	—	102
1935-36	—	—	—	—	—	—	2	2	—	—	2	—	6
1936-37	6	1	9	9	17	12	4	5	4	1	2	1	71
1937-38	—	2	1	1	3	7	6	2	1	—	—	—	25
1938-39	1	2	6	—	2	2	1	—	2	—	—	—	23
1939-40	—	—	—	—	1	—	—	—	1	3	1	—	6
1940-41	4	16	8	8	5	20	20	11	7	—	—	—	99
Total	46	64	119	121	112	111	81	52	31	20	19	16	792

reported by L. J. Schermerhorn, and numerous other American workers have established beyond doubt the efficiency of Phase I pertussis vaccine as a prophylactic against whooping cough. The dosages recommended and used by most of these workers are 70,000 million or 80,000 million organisms, divided into four doses and given subcutaneously into the deltoid, biceps or triceps regions at intervals of one week. I shall not bore you with figures of their experiments. Most of them have been so efficiently carried out with controls, and in such numbers that even a pathologist would be satisfied! The Grand Rapids experiments were made on 2,000 children vaccinated with Phase I vaccine and on 2,000 children enrolled as controls, and the observations were followed assiduously over a period of five years. The results of all these writers on the whole are very similar, and I shall attempt here to summarize the main conclusions, upon which all appear to be agreed:

1. Vaccine made from Phase I growth of the pertussis organism is essential to success.

2. For a lasting immunity large doses should be given—70,000 million to 80,000 million organisms.

3. The vaccine is best administered subcutaneously in four divided doses at intervals of one week.

4. Immunity was conferred within four months on approximately 85% of the children vaccinated. (Sauer states that the period is four months; Schermerhorn in the Grand Rapids experiment claims that immunity is built up earlier.)

5. The 15% of vaccine-immunized children who later contract the disease will have a milder attack than children who have not received the vaccine.

6. There is strong evidence that the protection conferred by active immunization in this way is similar to that of a previous attack of the disease.

7. The reactions from the vaccine, although never severe and occurring in 10% or less of cases, vary somewhat according to the make of the vaccine and of course according to the dosage.

8. The best period for immunization is in the second six months of the first year of life.

There are certain difficulties here in Australia, especially in private practice, which make the above procedure somewhat difficult to carry out: (i) The Australian has a natural antipathy towards injections of any sort, especially where his children are concerned. (ii) He likes to be given a 100% guarantee of protection. (iii) He takes a great deal of rousing before he will adopt any medical procedure, unless he is actually faced with the disease in his midst. (iv) He is strongly suspicious of reactions after injections. On account of these idiosyncrasies it may take a number of years yet before the members of the public will be persuaded to have their children protected against pertussis as a routine measure, even to the extent to which they have responded in the case of diphtheria. However, we can still do a great deal to protect children aged under three years once an epidemic arrives in the community. I am of the opinion that small repeated doses of Phase I vaccine, C strength, as supplied by the Commonwealth Serum Laboratories, given every second or third day in doses of 0.5, 0.75, 1.0 and 1.0 cubic centimetre, the total dosage being between 30,000 million and 40,000 million organisms, will build up a rapid immunity and will give protection to a very large percentage of children, even though these children are contacts, and will lessen the severity of the disease even if it does not completely protect them. This immunity will tide a child over the particular epidemic. He will be two or more years older by the time he is called upon to face another epidemic, and I accordingly advise all parents whose children have been treated in this way to give them the opportunity of two injections of the vaccine in two years' time or at the onset of the next epidemic. In this way I feel sure we can tide the majority of little children over the danger period of childhood. The reactions to this smaller dosage have, in my experience, been negligible. These dosages can be given to infants aged under six months, and they protect them during that extremely dangerous period of life.

Schermerhorn⁽¹⁰⁾ reports a controlled experiment showing the comparative value of convalescent serum and vaccine given before the onset of symptoms to directly exposed children. A direct exposure was defined as an intimate indoor family exposure; and no effort was made in any groups to keep the contacts away from the other children. Convalescent serum gave a 73% rate of protection; pertussis vaccine gave a 67% rate of protection; among unvaccinated controls the rate of protection was 18%.

Hamilton⁽¹¹⁾ reports a similar uncontrolled experiment with Phase I vaccine, and many infants and children in institutions have been protected from the spread of pertussis by the adoption of similar methods with Phase I vaccine at the onset of an outbreak in their midst.

As to the value of convalescent serum, Meader⁽¹²⁾ reports a 72% protection rate amongst exposed children who received 10 cubic centimetres of pooled convalescent serum soon after exposure; but if serum is given in the latter part of the incubation period, or once the disease has developed, no protection or benefit appeared to be gained. Cohen and Lapin⁽¹³⁾ (1930) report an 85% protection rate among exposed infants and children who are given 20 to 40 cubic centimetres of convalescent serum, and a 67% protection rate with hyperimmune serum in doses of 10 to 20 cubic centimetres. North and Anderson⁽¹⁴⁾ (1941) suggest the use of pooled human serum for the protection of contact babies when hyperimmune or convalescent serum is not available. As to the use of vaccine for the treatment of this condition once the disease has developed, no convincing records have been published.

I am of the impression that small repeated doses, as stated above, given on alternate days in the early stages of the disease, are of benefit, and should not be denied to children aged under two years who contract the disease. My own impression is that the number and severity of the spasms seem to decrease more rapidly under this treatment, and it is the number and severity of the spasms which in many cases are the determining factor between death and chronic ill health and lung damage on the one hand and recovery on the other hand.

From a review of the whole subject, so serious is this disease amongst little children, and so effective is the prophylaxis that Phase I pertussis vaccine will convey, that I would urge all medical men to avail themselves of this "life-protective" agent, no matter what their doubts have been in the past; and in particular I would urge those of you who deal with the education of the people in health and preventive medicine to do all in your power to make this fact known to the public. In this way it will not be very long before whooping cough will rank amongst those diseases which no longer scourge a well-regulated community.

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A NOTE ON THE CULTIVATION OF *HÆMOPHILUS PERTUSSIS*.

By PHYLLIS M. ANDERSON, M.B., M.R.A.C.P.,

From the Department of Bacteriology,
University of Sydney.

THE cough plate method for isolating *Hæmophilus pertussis* from whooping cough patients is not an elegant one, and difficulties are often encountered in dealing with infants, when the cough is weak, or in mild or suspect cases, in which the cough occurs chiefly at night.

The use of the post-nasal swab was suggested by W. L. Bradford and Betty Slavin, who published a small series of cases, comparing it favourably with the cough plate.

By the courtesy and cooperation of Dr. Vida Thompson, Registrar of the Royal Alexandra Hospital for Children, the technical procedure was tested on a number of infants and children attending the pertussis clinic at the out-patient department.

Flexible copper wire, gauge 19, was used in lengths of 15 centimetres, and on one end a tiny loop was made and dressed with a thin layer of cotton wool. These swabs were sterilized in tubes and were then ready for use. For the taking of the swab the child was seated on its mother's lap and the head was extended firmly against her shoulder. The manipulator bent over the child and passed the wire along the wider anterior nares into the post-nasal space. A side-to-side movement was then imparted to the swab and the finger could feel the tip passing over the posterior pharyngeal wall. It was then quickly withdrawn, the end of the swab being depressed slightly and describing an arc. The wire was usually found to have taken on a curved shape.

Swabs were taken from children as young as three months old and no difficulty was encountered; toddlers and older children occasionally coughed, but no failures occurred. The swabs were rubbed onto Bordet-Gengou medium containing 15% of horse blood and incubated for four days, and a satisfactory proportion of positive cultures was obtained. A comparison with the cough plate method was not made; but Bradford and Slavin state that the growth is frequently richer than on the cough plate and even sometimes pure.

Attention is drawn to the simplicity of the method, in the hope that in future epidemics cultures may permit of earlier diagnosis of infection of contacts, so that control of such children can be exerted at the period when they are most dangerous to their fellows.

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SOME OBSERVATIONS ON THE EFFECT OF SEDATIVE DRUGS ON THE "CARDIAZOL" CONVULSION.

By N. V. YOUNGMAN,
Brisbane.

PRIVATE practice presents many difficulties. Not the least is that of assessing the significance of phenomena observed in the natural history of a disease. Particularly is this the case when one is dealing with drugs. Practitioners cannot select their material as they wish nor employ therapy in modes other than those conforming to standard lines of treatment.

It was for these reasons that, after certain observations had been made during the treatment of patients with convulsant therapy, it was thought desirable to observe whether experimentation with guinea-pigs would assist in the investigation of these problems.

In psychiatry the need for sedative drugs has always been great, in order to secure adequate rest for the patient. The dose of these drugs given has often to be large, especially for excited patients, and when the necessary facilities for the adequate segregation of patients are not available. Since the introduction of shock therapy sedatives may also be needed to control certain unpleasant sensations or reactions associated with the induction of the convulsive seizure. These fall into three groups. First there is the presence of fear occurring before or at the time the injection is given. It arises more often if patients are allowed to discuss their treatment with each other, and it also becomes more prominent as the number of injections increases, even if there is complete amnesia for the initial injections. I well recall one woman asking placidly several hours after her convulsive seizure was over, when she was going to be given the injection, and yet before the subsequent injections she exhibited an increasingly severe degree of anxiety. It is difficult to believe that discussion alone is responsible for the development of this condition. Secondly, and perhaps the worst of these associated phenomena, is the production of a partial reaction. This is usually due to inadequate dosage and is a terrifying experience for the patient—so much so that he may refuse further treatment on these lines. This most frequently occurs when the commencing convulsant dose is being ascertained, or subsequently if fear is present, and then, I believe, it is the vascular changes associated with this state that make a previously convulsant dosage insufficient. Thirdly, confusional and excitement phases following the convulsive seizure may require the use of sedatives for their control.

Clinically it was found that when sedatives were given for these purposes the resulting reaction was often considerably modified. It may be inhibited entirely or partial reactions may occur with their untoward effects.

In the following experiments, an endeavour was made to see how different sedatives affected the convulsive seizure and to find whether the dose of "Cardiazol" could be anticipated which would constantly produce a reaction after the giving of any particular sedatives.

The following steps were taken: (i) The dose of "Cardiazol" which would produce a constant reaction in the guinea-pig was established. The relation of this dose to the lethal dose was then ascertained. (ii) The dose of sedatives which would produce a mild hypnotic effect on guinea-pigs was established. An endeavour was made to produce a comparable degree of sedation with each drug. (iii) The animals were then given the dose of sedative, and after they had reached a certain stage of recovery the basal convulsant dose of "Cardiazol" was given and the resultant reaction was noted. If no reaction occurred, then in similarly treated animals the dose of "Cardiazol" given was gradually increased.

Material.

The guinea-pigs used in these experiments were kindly made available by Dr. Derrick, of the Department of Pathology and Microbiology. They weighed, generally, between 400 and 500 grammes, received a standardized diet of pumpkin and lucerne, and were maintained under similar conditions. Altogether about 120 animals were used. The same animal was never used at intervals of less than one week, in order to ensure that the elimination of drugs had occurred in the interim. The injections were given intraperitoneally, because from my observation I am convinced that in an animal of this size absorption by this route is probably more constant and reliable than after intramuscular injections. The dose of the drugs was usually made up in about one cubic centimetre of water.

The Normal Guinea-Pig Reaction.

Watterson, in *The Journal of Mental Science*, September, 1939, describes the convulsive seizure in guinea-pigs after

the intramuscular injection of "Cardiazol". I have, in the main, adopted this classification, which is as follows. After the injection the animal continues to move about normally, although it may repeatedly sniff the cage while so doing, until the first manifestations of the reaction occur. The phases are: (i) jerking phase, (ii) crouching phase, (iii) racing phase, (iv) tonus phase.

Jerking Phase.

The jerking phase follows at intervals of one to ten minutes after the injection. It commences with a sudden upward and backward jerking movement of the head. This clonic movement at first may be isolated, or a short series of such movements may occur. They then become more frequent and merge into the second phase.

Crouching Phase.

In the crouching phase the whole body is involved. The animal crouches with its front legs extended and abducted. The previous clonic or jerky movements of the head involve the whole body. During this phase twisting and torsion of any part of the neck or body occur and the animal may topple onto its side or be forced backwards by the severity of the spasms. This phase lasts generally for half or one minute and is followed after a short quiet period by the third phase.

Racing Phase.

The animal becomes frenzied and races forward, unmindful of any obstacles in its path. It may squeal at the same time, but this more often signals the end of this phase. This may last up to twenty seconds, and the next stage follows within a few seconds.

Tonus Phase.

The animal lies on its side in opisthotonos with the limbs extended. A few typical clonic movements may occur, but usually the limbs move to and fro without any characteristic time relationship, and can perhaps best be described as if the animal were beating the air with its extended forelegs and kicking wildly with its hind limbs. After a varying period the animal regains consciousness, lying with its hind legs splayed out and its front legs abducted, respiration being shallow and rapid and its fur all ruffled. It finally resumes its normal activities.

Variations.

The following variations may occur: (i) Only jerking occurs. (ii) The crouching phase may not be followed by racing or the other phases. (iii) Several crouching phases may occur before the further stages of the reaction follow. These usually occur at intervals of five minutes. If tonus occurs, it rarely follows any but the last crouching phase. (iv) The tonus period varies considerably in length. It may be only a few seconds. It may be several hours, and if it is prolonged death usually follows. Further

investigation is necessary to determine whether permanent cerebral damage occurs commensurate with the length of this period. The length of these stages and their time relationships vary according to the size of the dose of "Cardiazol" and whether sedatives have been given beforehand; whence these variations are of greater diversity.

Comment.

Of the phases or stages the significant ones are jerking, crouching and tonus; any further reference to these words signifies that that stage of the reaction has occurred.

In this guinea-pig reaction, if crouching occurs, I regard it as equivalent to a major or good reaction. From the above description of the convulsive seizure it may appear that the stage of tonus should occur for such a reaction to be classified as major; but I believe that the crouching phase is more analogous to the tonic stage of a typical convulsion of so-called idiopathic clinical epilepsy.

Explanation of the Tables.

In the first column in all the tables the experimental number of the animal used is given. The animals were weighed preceding the injections, and this weight, in grammes, is given in the second column. The dosage of all drugs given was calculated according to the animal's weight. The individual volume and strength of the injected drug are not given.

The salient times occurring during the "Cardiazol" convulsive seizure were noted according to the phases jerking, crouching, further crouching and tonus.

With the sedative drugs three time periods are given. The first marks the time interval from the giving of the injection till the onset of ataxia. This was tested by attempting to move the hind limbs. Ataxia was present if there was lack of control and flaccidity of this part of the animal. The second period, "asleep", began when the animal toppled over onto its side asleep. The third time noted, "awake", occurred when the animal awoke, although it was often some time before it regained its normal range of activity. Thus in the tables these three periods are headed "ataxia", "asleep" and "awake".

When "Cardiazol" was given after the sedative the time interval on the tables is the period from the time of the initial injection of the sedative to the time of the injection of "Cardiazol". It is noted in hours and minutes.

Dosage of "Cardiazol".

Watterson showed that with a dose of 70 milligrammes per kilogram of body weight a constant reaction was obtained; but with smaller doses one could not be certain of obtaining a reaction in all cases.

The results (Table I) with this dosage show that the crouching phase occurs practically every time, but the tonus phase followed less constantly. Although a reaction is constantly produced, there are wide variations in the time intervals of the phases. With this dosage one of the sixteen animals died.

TABLE I.
Results of Injection of 70 Milligrammes of "Cardiazol" per Kilogram of Body Weight.

Experiment Number.	Weight of Guinea-pig. (Grammes.)	Interval (In Minutes) Before				Result.
		Jerking.	Crouching.	Further Crouchings.	Tonus.	
2	470	5	6	12	—	Recovery.
3	490	2½	3	5½	9½	Recovery.
4	460	4½	5½	10	15	Recovery.
5	460	—	7½	—	—	Recovery.
7	440	6	7½	15, 20	21	Recovery.
14	300	3½	5	12	—	Recovery.
15	420	1	2	4, 7	8½	Recovery.
17	430	6	7	13	—	Recovery.
19	390	8	9	—	—	Recovery.
20	420	4½	6½	—	7½	Recovery.
21	450	1½	2	4½, 8	—	Recovery.
22	470	—	—	—	—	Recovery.
23	450	6½	8	—	—	Recovery.
24	480	5	8	—	9	Recovery.
25	450	10	10	—	—	Recovery.
6	570	4½	7	15½, 20½	21	Death.

When the dose was increased to 75 milligrammes per kilogram of body weight (Table II) the interval between the phases was shortened and the onset of the reaction followed sooner after the injection than with the smaller dose. The mortality rate also increased, 10 out of the 19 animals dying.

With an increase to 100 milligrammes per kilogram of body weight (Table III), 11 out of the 12 animals died, and again the time periods between the phases were shortened. The lengths of the phases were reduced and became more constant.

From these observations one can regard the basal convulsant dose of "Cardiazol" for this type of guinea-pig reaction as 70 milligrammes per kilogram of body weight, and the nearer the dose approaches the lethal dose, the more constant the reaction becomes.

No attempt was made to find out if there is between the convulsant and lethal stage a dose of "Cardiazol" producing a reaction resulting in cerebral damage of a permanent nature, because pathological facilities for such an investigation were not available.

Effect of Morphine on the "Cardiazol" Convulsive Seizure.

Effect of Morphine on Guinea-Pigs.

The first dose of morphine injected was equivalent to 10 milligrammes per kilogram of body weight; but this had no obvious effect on the behaviour of the guinea-pig. After continuing with its normal activities for a short time after the injection, the guinea-pig sat still; but if it was touched or disturbed it would move about the cage with very actively executed movements for a few seconds before resuming its sitting position.

With an increased dosage to 80 milligrammes per kilogram of body weight again no great change in behaviour was apparent. The guinea-pig sat still, respiration was unaffected, the abdomen was distended and tympanitic, and if an endeavour was made to move the animal it regained as quickly as possible its sitting position. The rapidity with which this was done marked the main difference produced by the two doses of morphine, as far as overt behaviour was concerned. Even these doses are large, compared on a weight standard with those given clinically, and so it was thought that results would not be significant if a further increase in dosage was made in order to gain some degree of narcosis, although such experiments may help in investigating the basic mechanisms of the convulsive process.

Result of "Cardiazol" Injection following Morphine.

The basal convulsant dose of "Cardiazol" given after the smaller dose of morphine produced a reaction similar to a good reaction in the control series. After the larger dose of morphine the reaction was similar to that occurring after the big dose of "Cardiazol", in that the convulsive seizure occurred sooner after the injection and the time relationship of the different stages was more constant. Five of the 14 animals in this series died.

Discussion of Experiments.

These experiments suggest that morphine does not dampen the effect of "Cardiazol", but that, particularly after larger doses of morphine, the animal is more sensitive to the action of "Cardiazol" and that there is a lowering of the convulsive threshold of the latter drug.

TABLE II.
Results of Injection of 75 Milligrammes of "Cardiazol" per Kilogram of Body Weight.

Experiment Number.	Weight of Guinea-pig. (Grammes.)	Interval (in Minutes) Before				Result.
		Jerking.	Crouching.	Further Crouchings.	Tonus.	
77	440	4	5½	15	—	Recovery.
78	500	5	7	20	21	Recovery.
81	430	6	9	—	—	Recovery.
82	410	4	5	—	—	Recovery.
85	480	4½	5½	—	—	Recovery.
86	470	2½	4	—	—	Recovery.
88	530	6	7	—	—	Recovery.
99	450	—	1½	8	—	Recovery.
100	450	1½	2	—	3	Recovery.
8	460	5	5½	10	12	Death.
9	470	1	1	6	6½	Death.
10	520	3	4½	6	8½	Death.
79	500	4	6½	13½	14	Death.
80	490	2	2	5, 6	9½	Death.
97	410	4	3½	11½	12	Death.
198	430	1½	2	5	12	Death.
194	460	2½	4½	—	5½	Death.
195	390	1½	2	4	5½	Death.
196	450	4	5	11	11½	Death.

TABLE III.
Results of Injection of 100 Milligrammes of "Cardiazol" per Kilogram of Body Weight.

Experiment Number.	Weight of Guinea-pig. (Grammes.)	Interval (in Minutes) Before				Result.
		Jerking.	Crouching.	Further Crouchings.	Tonus.	
150	510	2	3½	8½	9½	Recovery.
151	480	1½	3½	—	3	Death.
152	480	1½	2½	—	4	Death.
153	480	1½	2½	—	6	Death.
154	480	1½	2	—	2½	Death.
155	440	3	4½	6½	7½	Death.
180	450	3	4	10½, 16½	17	Death.
181	420	4½	7	14, 21½	22	Death.
182	480	3	4	15	15½	Death.
183	380	3	5	9½, 12½	13	Death.
184	390	4½	12½	—	13	Death.
185	470	4	5	—	6	Death.

TABLE IV.
Results of Injecting "Cardiazol" (70 Milligrammes per Kilogram of Body Weight) after a Preliminary Injection of Morphine.

Experiment Number.	Weight of Guinea-pig. (Grammes.)	Dose of Morphine. (Milligrammes per Kilogram.)	Time of "Cardiazol" Injection After Morphine.		Interval (in Minutes) Before				Result.
			Hours.	Minutes.	Jerking.	Crouching.	Further Crouchings.	Tonus.	
50	450	10	2	35	6	20	—	—	Recovery.
72	430	10	2	29	3	4½	—	—	Recovery.
73	440	10	2	38	6	8	—	—	Recovery.
91	560	10	2	47	—	—	—	—	Recovery.
90	480	10	2	30	4	7½	18	—	Recovery.
49	410	10	2	14	6	—	—	—	Recovery.
89	590	10	2	26	6	7	—	—	Jerks for half an hour.
11	460	10	2	30	—	10	—	10½	Prolonged crouching.
71	400	10	2	13	4	6	13	—	Death.
74	420	10	2	44	2	3	—	6	Death.
40	430	80	2	37	5	10	—	11	Recovery.
47	550	80	2	60	4½	6	—	—	Recovery.
48	470	80	2	13	4	6	—	—	Recovery.
134	450	80	2	29	2½	6	—	—	Recovery.
135	460	80	2	47	1½	5	—	—	Recovery.
136	450	80	2	46	3	5	—	6	Recovery.
75	410	80	2	9	1½	3	—	—	Prolonged crouching.
93	450	80	3	01	3	6	—	—	Recovery.
132	450	80	2	22	1½	—	—	—	Prolonged crouching.
76	390	80	2	15	3	6	—	10	Prolonged jerking.
92	450	80	2	54	2½	3½	9	9½	Death.
94	470	80	3	11	3½	5	9½	10	Death.
133	460	80	2	32	2	4	10½	11	Death.
137	440	80	2	46	4	6	—	6½	Death.

From the tables one gathers that the reaction following the use of morphine was of the normal type, and the time relationship, if altered, depended on the preceding dose of morphine. However, from my observation of these animals there also appears to be a variation in the phenomena of the reaction. There appears to be an increase in the motor component of the convulsive seizure, both in the degree of activity and in the variety of the motor characteristics. It is unfortunate that one cannot observe other features of the convulsive seizure, as these assume importance when one considers on the clinical material the relationship of this drug with them. It would not appear unreasonable to conclude that all the manifestations of the convulsive seizure would be similarly affected.

To summarize, one may say that morphine lowers the convulsion threshold of "Cardiazol" and probably distorts as well as increases the activity of the ensuing reaction.

Clinical Observations and Correlation with Experimental Findings.

1. Morphine and hyoscine have been used to allay fear associated with the giving of the "Cardiazol" injection. In a number of cases this proved satisfactory. The experimental work suggests that this procedure would make more certain the possibility that a complete convulsive seizure will occur and so eliminate partial reactions. This fact would then suggest the advisability of giving morphine and hyoscine as a routine measure; but there are unfortunately certain objections. In some cases, particularly when the patients are worried and when large doses of morphine are used, the patients may appear to be unaware of the "Cardiazol" injection, but will afterwards state that the fear was not abolished. In other cases, although this procedure may banish the fear of the injection, the post-convulsive stages are even more unpleasant than they are if morphine and hyoscine had been withheld. One can only speculate as to whether this is due to the action of morphine and hyoscine in altering rather than heightening the effect of the "Cardiazol".

2. Morphine is also used between the incidents of "Cardiazol" treatment for the control of depressed and restless patients. I believe that in certain cases, when this measure is adopted and "Cardiazol" injections are given (normally three per week), a typical variety of mental confusion develops. This is characterized by a severe alteration of the memory component. In mild cases it particularly involves recent events; but at the height of the confusion the patient may be unable to recall

such things as what had been eaten a few minutes previously, or the number and ages of her children. At the same time the patients are usually quite cheerful and become apprehensive if one persists in closely questioning them rather than confining the conversation to generalities. Further investigation is needed to determine whether permanent cerebral damage would result from persistence in such treatment. We must regard the confusion as a result of therapy rather than as a result of the initial mental condition.

3. Morphine and hyoscine have also been given to control post-convulsive states, especially excitement. When this is done, and particularly if the excitement is not controlled by the first dose and further injections are given, in some cases the restlessness so increases as to produce a state of mania. This abnormal state may last several days. The patient may benefit from it and be amnesic for this period. One can perhaps regard this state as similar to the heightened reactions occurring in the experimental work, although then only the motor aspect of the convulsion is studied.

Conclusions.

I believe that the use of morphine, especially in large doses, is inadvisable during convulsant therapy, owing to the increased effect of the "Cardiazol" in such cases, and also because the convulsive seizure in its various manifestations is altered. Its use should be perhaps confined to a smaller percentage of patients who have an extreme fear of receiving an injection.

Effects of Hyoscine Hydrobromide on the "Cardiazol" Convulsive Seizure.

Effect of Hyoscine Hydrobromide on the Guinea-Pig.

Doses of hyoscine hydrobromide of one-tenth, one and two milligrammes per kilogram of body weight were given. For a short period after the injections the animals moved about normally and then sat still and would move only when disturbed. The results were similar to those produced by morphine, and it appears that these two drugs have much the same effect on the guinea-pig.

Result of Injection of "Cardiazol" following Hyoscine (Table V).

In all cases complete reactions occurred after the injection of "Cardiazol" and the results were similar to those with morphine, in that the reaction occurred more constantly and was heightened, variations occurred and the mortality rate was increased irrespective of the size of the preceding dose of hyoscine.

TABLE V.
Results of Injecting "Cardiazol" after a Preliminary Injection of Hyoscine (One-tenth of a Milligramme per Kilogram of Body Weight).

Experiment Number.	Weight of Guinea-pig. (Grammes.)	Dose of "Cardiazol". (Milligrammes per Kilogram.)	Time of "Cardiazol" Injection after Hyoscine.		Interval (in Minutes) Before				Result.
			Hours.	Minutes.	Jerking.	Crouching.	Further Crouchings.	Tonus.	
210	470	70	2	36	7	10	—	11	Recovery.
213	440	70	2	56	3	5	—	5½	Recovery.
214	490	70	3	03	5	6	—	—	Recovery.
215	560	70	3	04	2	4½	—	5	Recovery.
230	380	70	2	03	5	6½	13½	—	Recovery.
231	380	70	2	03	5	6	14	21	Recovery.
232	400	70	2	19	7	9	—	—	Recovery.
234	460	70	2	25	6	7	18	18½	Recovery.
236	470	70	2	32	4½	5½	12½	13	Recovery.
237	430	70	2	42	4	6	—	—	Recovery.
238	360	70	2	44	9	13½	—	—	Recovery.
239	520	70	2	54	1	1½	—	5	Recovery.
168	560	70	1	54	7	13	—	—	Recovery.
169	400	70	1	58	3	9	—	—	Recovery.
172	420	70	2	27	4½	7	7½	9	Recovery.
173	560	70	2	35	3½	7	—	—	Recovery.
206	400	70	2	23	4½	5½	14½	—	Recovery.
209	460	70	2	41	5½	6	14½	—	Recovery.
211	420	70	2	47	4	5	9½	10	Death.
228	430	70	1	53	1	3	—	6½	Death.
229	380	70	1	55	3½	4½	8½	9	Death.
233	380	70	2	19	2½	4	—	5½	Death.
235	510	70	2	31	5	6	17	18	Death.
204	520	70	2	17	1½	—	—	5½	Death.
206	570	70	2	14	6	12½	—	13	Death.
207	480	70	2	32	2	2½	6½	7	Death.
208	480	70	2	40	1½	2½	5½	6	Death.
170	460	80	2	03	6	9½	—	9½	Death.
171	460	80	2	26	5	5	13	13½	Death.

Conclusions.

Clinically I have given hyoscine alone only to control the reactions following the injection of "Cardiazol"; but it proved ineffective. I have used it frequently combined with morphine for the other indications given previously; but the results with this combination are identical. The experimental work then suggests that the action of these two drugs on the "Cardiazol" convulsive seizure is similar.

Effects of "Sodium Amytal" on the "Cardiazol" Convulsive Seizure.

Effect of "Sodium Amytal" on the Guinea-Pig.

The first dosage of "Sodium Amytal" tried was equivalent to 80 milligrammes per kilogram of body weight. This produced a satisfactory degree of narcosis, as will be seen in Table VI. The animal became ataxic approximately eight minutes after the injection. Eight minutes later

TABLE VI.
Results of Injecting "Cardiazol" after a Preliminary Injection of "Sodium Amytal" (80 Milligrammes per Kilogram of Body Weight).

Experiment Number.	Weight of Guinea-pig. (Grms.)	Interval after Injection of "Sodium Amytal" Before				Dose of "Cardiazol". (Milligrammes per Kilo-gram.)	Time after "Sodium Amytal".		Intervals (in Minutes) Before				Result.
		"Ataxia" (Mins.)	"Asleep" (Mins.)	"Awake."			Hours.	Mins.	Jerking.	Crouching.	Further Crouchings.	Tonus.	
				Hours.	Mins.								
13	520	11	14	3	56	70	4	06	—	—	—	—	No reaction.
29	410	15	18	1	03	70	2	25	—	—	—	—	No reaction.
30	450	13	20	1	00	75	2	25	—	—	—	—	No reaction.
31	460	11	23	1	52	75	3	13	—	—	—	—	No reaction.
51	410	10	19	1	43	75	3	14	7	8	—	—	Reaction.
52	400	10	16	1	08	75	3	25	—	—	—	—	No reaction.
53	430	14	26	1	37	75	3	38	—	—	—	—	No reaction.
54	430	4	6	1	36	80	3	48	4½	5½	15½	16½	Reaction.
108	460	5	7	1	20	80	2	40	10	18½	—	—	Modified reaction.
112	490	6	11	2	10	80	2	59	—	—	—	—	No reaction.
113	440	7	16	1	39	80	2	45	—	—	—	—	No reaction.
110	470	10	21	2	13	85	3	26	—	—	—	—	No reaction.
111	460	10	22	2	17	85	3	19	—	—	—	—	No reaction.
124	450	7	16	1	31	90	2	09	—	—	—	—	No reaction.
125	400	8	19	1	20	90	2	21	—	—	—	—	No reaction.
121	360	8	23	1	35	95	2	37	22	—	—	—	Jerking for two mminutes.
123	470	8	17	1	33	95	2	44	2	—	—	—	Jerking for five minutes.
160	460	6	22	1	36	100	2	48	—	—	—	—	No reaction.
161	430	7	18	1	25	100	2	53	3½	5½	10	11½	Recovery.
159	410	7	18	1	15	100	2	34	6	7½	—	—	Reaction.
120	450	8	13	1	58	100	2	56	2	3	—	—	Modified crouching.
122	370	7	16	1	34	100	3	03	4	10	—	—	Modified crouching.
154	450	9	16	1	21	100	2	19	5	6	13	—	No racing.
154	460	5	11	1	34	100	2	31	10	11	20	—	No racing.
157	530	7	12	1	20	100	2	08	6	9	—	—	Racing.
168	400	9	16	1	31	110	2	20	—	—	—	—	No reaction.
191	430	3	5	1	26	110	2	03	1½	2	6, 8, 11, 13, 15, 17	—	Reaction.
192	440	12	20	1	38	110	—	—	—	—	—	—	No reaction.
189	430	8	17	1	32	110	2	17	—	13½	—	—	Crouched for one-quarter minute.
190	430	5	16	1	42	110	2	12	—	15	—	—	Crouched for one-quarter minute.
188	490	7	10	1	27	120	2	27	1	1½	4	8	Death.
187	500	11	17	1	45	120	2	19	1	2	7	9	Death.

it fell on its side asleep. This state lasted about eighty minutes, and was followed by a period of unsteadiness and weakness before complete recovery occurred. The degree of narcosis was not very deep, for the animals were readily aroused by such stimuli as being placed in the hot sun or manually moved into another position. As the reaction was fairly constant the animals must be regarded as being in a comparable state when each injection of "Cardiazol" was given.

Effect of "Sodium Amytal" on the Convulsive Seizure.

From the basal convulsion dose of "Cardiazol" of 70 milligrammes per kilogram of body weight gradually increasing doses were given to a maximum of 130 milligrammes per kilogram of body weight. It will be seen from Table VI that there are wide variations in the resulting reaction. In 16 of the 33 animals no reaction at all resulted. This occurred less often with the large doses, but even then there was no certainty that a reaction would ensue. However, the possibility of a reaction was more likely the closer the dose of "Cardiazol" approximated to the lethal dose.

The type of reaction also showed considerable variations. It was most often confined to the jerking and crouching phases. The racing and tonic stages were uncommon. If only jerking occurred, the animal's activities were hardly interrupted, the movements being much less powerful than in the control series. When crouching occurred, this too was less active and shorter in duration. It appeared to cause the animals little discomfort. Thus in some cases the animals were chewing pumpkin, and this activity was immediately resumed after the jerking or crouching occurred, whereas in normal animals a considerable period elapsed before the feeding was continued.

Not only the convulsive episodes, but also the times between the phases varied widely. Usually there was a tendency for the initial movements to be delayed, and the length of the active phases was diminished.

Several other features call for comment. One is that the preliminary dose of "Sodium Amytal" appears to increase the tolerance to "Cardiazol", for no death occurred in this series till the dose reached 120 milligrammes per kilogram of body weight. In another series it would be worth while to observe, if more animals were given this

dose, whether it constantly produced death. In all cases when the after-effects of the sedative were still present at the time when the "Cardiazol" was given, and even when no reaction occurred, the "Cardiazol" appeared to hasten the animal's return to normality.

Effect of "Sodium Amytal" on the Convulsive Seizure in Clinical Practice.

Clinical case reports show that although "Sodium Amytal" lessens the likelihood of a reaction, this may occur. It is impossible to foresee when this will happen.

Conclusions.

These experiments suggest that one cannot be certain that a convulsive seizure will occur if "Sodium Amytal" has been given beforehand, even if large doses of "Cardiazol" are used. Another purpose for "Cardiazol" is, however, suggested, in that it may be useful to combat overdosage or other side-effects of "Sodium Amytal".

Effect of Phenobarbitone on the "Cardiazol" Convulsive Seizure.

Effect of Phenobarbitone on Guinea-Pigs.

The initial dose of phenobarbitone given was 80 milligrammes per kilogram of body weight, the same dose as had proved satisfactory with "Sodium Amytal". The stages of "ataxia", "sleeping" and "awake" were reached approximately 60, 40 and 160 minutes after the injection of the phenobarbitone. These time intervals would suggest that phenobarbitone was much more effective than "Sodium Amytal"; but there is little actual difference in their actions with this dosage. With phenobarbitone there is a longer latent period before its narcotic action becomes manifest. The "sleep" stage is also more slightly delayed. It is no deeper, for the animals can again be readily aroused with moderate stimuli and then relapse into their sleeping state.

Effect of "Cardiazol".

From Table VII it will be seen that no semblance of reaction to "Cardiazol" occurred till twice the basal convulsant dosage had been given. Even then a reaction occurred in only one case, and this was extremely modified. It took place at a long interval after the injection and temporarily interrupted the animal's feeding. Again the

TABLE VII.
Results of Injecting "Cardiazol" after a Preliminary Injection of "Luminal Sodium" (80 Milligrammes per Kilogram of Body Weight).

Experiment Number.	Weight of Guinea-pig (Gms.)	Interval After Injection of "Luminal Sodium" Before		Dose of "Cardiazol" (Milligrammes per Kilogram.)		Time After "Sodium Amytal".		Interval (in Minutes) Before				Result.
		"Ataxia." (Minutes.)	"Asleep." (Minutes.)	"Awake." Hours.	"Awake." Minutes.	Hours.	Minutes.	Jerking.	Crouching.	Further Crouching.	Tonus.	
12	400	30	40	2	15	70	2	45	—	—	—	Hastened recovery.
26	425	24	28	1	25	70	2	15	—	—	—	Hastened recovery.
66	320	12	32	2	26	70	3	15	—	—	—	Hastened recovery.
27	430	25	50	1	35	75	3	40	—	—	—	Hastened recovery.
28	385	20	35	1	48	75	3	54	—	—	—	Hastened recovery.
64	410	14	34	3	31	75	3	34	—	—	—	Hastened recovery.
63	460	17	40	2	06	80	2	47	—	—	—	Hastened recovery.
65	450	14	38	1	33	80	3	00	—	—	—	Hastened recovery.
325	390	11	34	2	43	90	3	26	—	—	—	Hastened recovery.
326	428	12	32	2	08	90	3	20	—	—	—	Hastened recovery.
334	420	14	28	2	50	90	3	25	—	—	—	Hastened recovery.
329	400	16	22	3	21	100	3	33	—	—	—	Hastened recovery.
332	340	14	25	2	24	110	3	24	—	—	—	Hastened recovery.
328	350	16	31	3	22	110	3	46	—	—	—	Hastened recovery.
336	380	17	22	2	39	110	3	23	—	—	—	Hastened recovery.
333	420	20	31	3	46	120	3	56	—	—	—	Hastened recovery.
330	370	15	26	3	25	120	3	54	—	—	—	Hastened recovery.
335	400	17	27	3	29	140	4	00	—	—	—	Very modified recovery.
331	380	13	26	4	07	160	4	19	2	2½	5, 7, 9½, 13, 23	Recovery.
327	360	13	28	3	45	160	4	20	—	—	—	Recovery.
349	480	18	26	2	03	200	2	51	1	1½	5, 7, —, 20	Recovery.
350	480	16	32	2	12	200	2	54	—	4½	6½, 8½, 11, 13, 15	Recovery.
351	440	15	24	2	31	200	3	08	—	9	24	Recovery.
352	450	14	23	2	53	200	3	27	1½	2	4½, 6½, 8½, 12½	Recovery.
353	560	13	22	2	27	200	2	54	—	1½	3, 4½	Recovery.
354	400	11	20	2	05	200	2	58	—	4½	—	Recovery.

"Cardiazol" appeared to hasten the recovery from the after-effects of the sedative, although this effect did not appear to be as pronounced as with the other barbiturates.

When the dose of "Cardiazol" was raised to 200 milligrammes per kilogram of body weight (that is, twice the lethal dose and nearly three times the basal convulsant dose), a reaction was obtained in each case. This showed many unexpected and interesting features. The reaction, in the main, consisted of a large number of crouching phases (in one case 13), following each other at very short intervals. The motor component of these phases was not dampened to the degree which might have been anticipated. They occurred at much more frequent intervals than in any of the other experiments. Despite them, the tonic stage occurred in only one instance, whereas usually over the whole of the series, if two or more crouching phases occurred, the tonic stage followed.

Another remarkable feature was that after the reaction was complete the animal's behaviour was strange, being characterized by such changes as forcibly chewing the wire bars of their cage, jumping unheedingly over each other, attempting to climb out of the cages, repeatedly shaking their heads, and being extremely restless. One can perhaps best describe this behaviour as that of an "excited confusion"; it persisted for about an hour.

It was also surprising that no death occurred, despite the large doses of "Cardiazol" given and the severity of the reaction which followed.

Conclusions.

From the clinical action of phenobarbitone in the convulsive disorders it might have been expected to have a similar effect on the "Cardiazol" convulsive seizure. This is substantiated in the experimental findings. Even when the usual dose is actually twice the normal dose of "Cardiazol" the convulsive seizure is entirely inhibited.

With very large doses a peculiar reaction results, characterized by prolonged repeated crouching and confusion. Of all the animal reactions seen in this series, it most nearly resembles those partial reactions which, occurring in clinical practice, have excitement as the main feature.

Another interesting result is the pronounced increase in tolerance to "Cardiazol" after the giving of phenobarbitone. The physiological explanation of the mechanism behind these reactions needs fuller investigation.

Effect of "Nembutal" on the "Cardiazol" Convulsive Seizure.

Effect of "Nembutal" on Guinea-Pigs.

A dose of "Nembutal" of 80 milligrammes per kilogram of body weight was first given, as this dose had proved adequate with the other barbiturates used. With this dose the death rapidly occurred of 10 out of the 12 animals. The dose was then halved, and this again produced a degree of narcosis deeper than that desired. Twelve animals were then given amounts of 20 milligrammes per kilogram of body weight. Although this produced ataxia, a very short period of narcosis occurred only in a few instances. None of these animals achieved a comparable state with that obtained with the other barbiturates.

Effect of "Cardiazol" after "Nembutal" (Table VIII).

In several instances, whilst the animals were still asleep from the large dose of "Nembutal", "Cardiazol" was injected. No change could be detected in the animals' behaviour. Furthermore, when the "Cardiazol" was given after the animals had awakened, no reaction or at the most a very slight reaction occurred. After the smaller dose of "Nembutal", "Cardiazol" had an effect comparable with that in the control series, except that there was an increase in the mortality figures.

TABLE VIII.
Results of Injecting "Cardiazol" after a Preliminary Injection of "Nembutal".

Experiment Number	Weight of Guinea-pig. (Gms.)	Dose of "Nembutal". (Milligrammes per Kilogram.)	Interval after Injection of "Nembutal" Before				Dose of "Cardiazol". (Milligrammes per Kilogram.)	Time after "Nembutal".		Interval (in Minutes) Before				Result.
			"Ataxia."	"Asleep."	"Awake."			Hours.	Minutes.	Jerking.	Crouching.	Further Crouchings.	Tonus.	
					Hours.	Minutes.								
252	460	80	2	2½	—	—	—	—	—	—	—	—	—	Death.
254	440	80	4	9	—	—	—	—	—	—	—	—	—	Death.
255	450	80	4	8	—	—	—	—	—	—	—	—	—	Death.
256	440	80	5½	6½	—	—	—	—	—	—	—	—	—	Death.
258	440	80	4	6	—	—	—	—	—	—	—	—	—	Death.
260	370	80	3	5	—	—	—	—	—	—	—	—	—	Death.
261	520	80	4	5	—	—	—	—	—	—	—	—	—	Death.
262	410	80	3	6	—	—	—	—	—	—	—	—	—	Death.
263	350	80	2	3½	—	—	—	—	—	—	—	—	—	Death.
263	450	80	3	4	—	—	70	4	—	—	—	11, 14½	—	Death.
269	510	80	4½	9½	—	—	70	24	—	—	—	—	—	No reaction.
257	550	80	4½	5½	—	—	70	24	—	2	2	—	3	Died after spasms.
279	400	40	2	4	6	49	—	—	—	—	—	—	—	Modified crouching.
281	450	40	2	3	6	46	—	—	—	—	—	—	—	Modified crouching.
282	440	40	2	3	6	45	—	—	—	—	—	—	—	Modified crouching.
276	480	40	3	7	5	02	100	5	59	—	—	—	—	Modified crouching.
277	420	40	2	6	5	01	100	1	47	—	—	—	—	Modified crouching.
278	450	40	1	8	3	35	80	5	31	—	—	—	—	Modified crouching.
280	340	40	3	4	4	58	100	5	48	1½	2½	—	—	Modified crouching.
356	350	20	9	—	—	—	70	3	33	2	3	9, 15	15½	Recovery.
357	360	20	15	—	—	—	70	3	37	—	11	—	—	Recovery.
355	340	20	16	—	—	—	70	3	33	3	5	11, 14½, 22	22½	Death.
359	410	20	6	—	—	—	70	3	51	5	6	9	9½	Death.
360	390	20	11	—	—	—	70	3	52	1½	2	3½	5	Death.
361	370	20	10	—	—	—	70	3	57	4½	5½	6½	7½	Death.
358	390	20	10	—	—	—	100	3	42	—	9	10½	—	Recovery.
364	370	20	5	15	—	37	100	4	00	1	2	5	6	Death.
365	410	20	4	12	—	36	100	4	00	2	2½	5	6	Death.
366	350	20	2	—	—	—	100	4	03	—	10	18	18	Death.
362	430	20	9	16	—	41	100	3	57	1	1½	4	5	Death.
363	360	20	6	18	—	36	100	3	57	1	2	—	2	Death.

Conclusions.

These experiments indicate that "Nembutal" in the guinea-pig does not react in the same way as the other barbiturates. There is, however, a common feature, in that if narcosis is produced the convulsive reaction is modified.

Effect of Chloral Hydrate and Sodium Bromide.**Effect of Chloral Hydrate and Sodium Bromide on the Guinea-Pig.**

Injections of chloral hydrate and sodium bromide were commenced with the dosage of 400 milligrammes per kilogram of body weight of each drug. As can be seen from Table IX, this produced a deep stage of narcosis. The dose was then lessened to 160 milligrammes of each drug per kilogram of body weight; the resultant effect was more in keeping with the desiderata. It was similar to that produced with the "Sodium Amytal". The halving of the dose to 80 milligrammes of each drug per kilogram of body weight produced excitement without narcosis.

Effect of "Cardiazol" following Chloral Hydrate and Sodium Bromide.

Irrespective of the dose of chloral hydrate and sodium bromide, the effect of "Cardiazol" was extremely variable. From Table IX it will be seen that the reactions were sometimes delayed. The jerking stage may not precede the crouching phase; the latter was often very short and the clonic movements were very feeble. There appeared to be no increased tolerance to the drug. Death often occurred at a considerable period after the reaction had taken place, and in a few cases it was not preceded by any convulsive reaction.

Conclusions.

Similar results occur in clinical practice. No reaction occurs, or only a modified reaction, till excretion of the drugs has taken place.

Effect of Paraldehyde on the "Cardiazol" Convulsive Seizure.

No experiments were made with paraldehyde, because its rationale in clinical practice of the type under review seems well established. Furthermore, it is extremely doubtful whether intraperitoneal injections would prove a suitable mode of administration. In the human patient up to six drachms of this drug can be given orally on the

night preceding "Cardiazol" treatment without the lessening of the chances that a convulsive seizure will occur. However, if a second dose is given approximately an hour before the injection, a reaction may not follow. This usually can be anticipated, because the patients are cold and vascular stasis is present. In my opinion, these factors rather than direct intracerebral change account for the untoward effect.

In my own practice three drachms of paraldehyde are given immediately before the "Cardiazol" injections as a routine measure in many cases. Not only does this technique lessen the frequency of post-convulsive excitement, but also the patients find this procedure more pleasant, despite the taste of the drug. Whether this beneficial result can be attributed to the prolonged sleep, allowing cerebral changes to return to normal before the patient wakes, or to an alteration in the reaction, one cannot be certain.

Undoubtedly paraldehyde is the most useful narcotic drug for use during shock therapy. Its ill effects are few, and fortunately can usually be foretold from the clinical state of the patient.

Discussion.

In the assessment of the value of any experimental work there is the inevitable difficulty of deciding whether reactions occurring in animals are comparable with those noted in clinical material.

It would at first appear that the reaction here described in guinea-pigs does not bear a close resemblance to that following the intravenous injection of the drug in clinical practice. However, closer analysis shows that this inference is unsound. If "Cardiazol" is injected into human muscle, after a latent interval a few clonic jerks occur, perhaps confined to one limb or even to part of a limb. These jerks gradually become more constant and widespread until the preliminary tonic stage occurs and is followed by the clonic stage of a typical convulsive seizure. The motor behaviour of this reaction is very similar to the guinea-pig reaction up to the onset of the "crouching" phase. There is not sufficient material to discuss the relationships of the "racing" and "tonus" phases of the experimental work to the clinical reaction, nor the mental changes associated with the slower clinical convulsive seizure. But it may be assumed from the clinical and experimental evidence that the type of the reaction largely

TABLE IX.
Results of Injecting "Cardiazol" after a Preliminary Injection of Chloral Hydrate and Sodium Bromide.

Experiment Number	Weight of Guinea-pig. (Grms.)	Sodium Bromide and Chloral Hydrate, Amount of Each, (Milligrammes.)	Interval after Injection of Drugs Before				Dose of "Cardiazol", (Milligrammes per Kilogram.)	Time after Sedative Drugs.		Interval (in Minutes) Before				Result.
			"Ataxia." (Minutes.)	"Asleep." (Minutes.)	"Awake."			Hours.	Minutes.	Jerking.	Crouching.	Further Crouchings.	Tonus.	
					Hours.	Minutes.								
267	430	400	2	21	3	16	70	4	13½	—	—	—	—	No reaction.
270	470	400	5	10	4	35	70	5	14	—	—	—	—	No reaction.
273	370	400	3	5	3	00	70	4	56	—	—	—	—	No reaction.
275	490	400	5	10	4	01	70	5	00	—	—	—	—	No reaction.
266	430	400	3½	19½	4	02½	70	4	30	6	49	—	—	Modified crouching.
271	389	400	3	4	4	03	70	4	35½	3½	4½	—	—	No racing.
285	620	400	3	4½	4	18	100	6	59	—	—	—	—	Death.
269	450	400	2	3	3	46	100	6	57	7	19	22	—	No racing.
272	460	400	1	2	3	10	100	6	07	9	9½	18	—	Death.
268	430	400	1	3	—	—	110	7	13	—	—	—	—	Death.
299	450	160	17	26	1	03	100	2	05	2½	4	15	—	No racing.
303	430	160	3	5	—	59	100	2	31	1½	2½	4	8½	Recovery.
304	470	160	1	3	1	07	100	2	48	1	1½	4	5	Death.
302	500	160	3	5	1	00	110	2	27	—	27	—	—	Modified crouching.
300	420	160	3	5	1	12	110	2	11	3	8	—	—	Recovery.
301	470	160	8	21	1	06	110	2	20	—	1½	—	6½	Death.
306	500	80	—	—	—	—	70	2	41	—	2	—	7	Recovery.
310	490	80	—	—	—	—	70	2	54	2	3	—	4, 7	Death.
308	490	80	—	—	—	—	70	2	46	—	3	—	—	No reaction.
305	550	80	—	—	—	—	85	2	25	—	—	—	—	No reaction.
309	380	80	—	—	—	—	100	2	50	23½	—	—	—	No reaction.
311	540	80	—	—	—	—	110	2	58	—	27	—	—	Modified crouching.
307	450	80	—	—	—	—	110	2	43	1½	1½	—	2	Death.

depends on the rate of introduction of the drug into the circulation. If this follows the intravenous route, the progressive march of events leading up to the major reaction is crowded into a relatively insignificant short stage before the major manifestation occurs, whereas with the slower absorption of the drug the earlier changes assume greater prominence. The method of intraperitoneal injection gives an opportunity to demonstrate a wider variety of epileptiform phenomena, depending on the dosage of the convulsant. The larger the dose, the closer the resemblance to the reaction that follows intravenous administration.

The slowly developing reaction is more useful in this work because it provides a number of phases. It is possible to estimate far more accurately the effect of the various drugs by noting how many of these phases follow after the convulsant dose is given.

Criticism may be levelled at the doses of the sedatives used. However, in the main the narcotic effects obtained with the barbiturates and chloral hydrate and sodium bromide appear to be comparable with those following their exhibition in clinical work. The effect of morphine and hyoscine is dissimilar; but even so, modification of the "Cardiazol" reaction occurred. These results have been previously discussed under the headings of the individual drugs.

Earlier in this paper it was mentioned that these experiments were made to see whether they would so substantiate certain clinical observations as to obviate the necessity for prolonged clinical trials, a procedure difficult in private practice. Their main purpose was (i) to see whether certain sedatives could still be used if convulsant therapy was indicated, and (ii) to observe whether they merely raised the threshold of the convulsant dosage.

In the main I believe this objective has been reached. It has been shown that the sedatives under review affect the convulsion in a fashion that cannot always be anticipated, and because of this inconstancy they should find no place in this type of therapy.

During the course of the investigation other interesting disorders of behaviour were noted, particularly associated with the convulsive states. Laboratory facilities would be required to permit an adequate investigation of the physiological basis of these reactions and the relation of the drugs to the convulsive mechanism. It would be helpful to record such experiments by film to allow a more careful study of the component movements of the reactions. Lack of these facilities compels this record to give the end results, with but an occasional intrusion into the speculative field.

It is an unfortunate feature of our present organization of medical practice that the opportunities for the carrying out of experimental work in conjunction with clinical practice are not readily available. Each medical centre should have experimental laboratories closely associated with the hospitals, so that the members of staffs and students would be able to utilize such facilities to give a more dynamic meaning to pathological processes. At present there is a tendency to think of them in terms of morbid anatomy and biochemical figures rather than as changes occurring in living units.

Conclusions.

1. The convulsive dose of "Cardiazol" for guinea-pigs by the intraperitoneal route closely approaches the lethal dose.
2. Guinea-pigs appear resistant to the hypnotic action of morphine and hyoscine if the drugs are given before "Cardiazol" injections; these drugs lower the convulsant threshold, heighten and distort the convulsive seizure and increase the mortality rate.
3. The barbiturates raise the convulsant threshold, lessen the activity of the various manifestations of the convulsive reaction and render "Cardiazol" less toxic to the guinea-pig. The degree of these effects varies with the different drugs of this group.
4. Whilst chloral hydrate and sodium bromide have a similar action to the barbiturates, their effects appear to be more variable.

5. Certain other interesting reactions occurring during these experiments are discussed.

6. In the main these experiments substantiate observations made during clinical work.

Acknowledgements.

I wish to thank Professor John Bostock for access to clinical material and for suggestions on this paper.

Reviews.

OBSTETRICS AND GYNÆCOLOGY.

In November, 1937, we reviewed the seventh edition of Aleck W. Bourne's "Synopsis of Obstetrics and Gynæcology". The eighth edition has now been published.¹ The book is what its title states—a synopsis—and, incidentally, a very good synopsis. Strangely, the part devoted to obstetrics precedes that on gynæcology; but this is because the first edition dealt with obstetrics only. The individual chapters are divided by cross-headings into various sections, and the details of the sections are set out in numbered paragraphs. As the book is intended to be used by students who are preparing for final examination, and by students and practitioners as a useful supplement to, and not a substitute for, the ordinary text-books, this form of presentation is satisfactory. The essential features are emphasized and the author states that in all controversial matters extreme views have been avoided. The general structure of the book may be judged from the following titles of the sections in the obstetric part: "Normal Pregnancy", "Abnormal Pregnancy", "Normal Labour", "Abnormal Labour", "The Puerperium and the New-Born Child", "Obstetric Surgery". A new sub-section on post-natal care is included in this edition. An attempt has been made to bring the subject matter up to date, and apparently with success. For example, the sex hormones are dealt with clearly and the use of sulphanilamide in various conditions is considered. There is an index which seems to be complete and will enhance the value of the book. Provided this book is used in the way that the author intends it to be used, both students and practitioners will find it valuable.

DISEASES OF THE VULVA.

DR. ELIZABETH HUNT has written her book in response to requests from general practitioners and gynæcologists for a text-book on vulval affections from the standpoint of the dermatologist. It is based on personal observation and study of over 1,000 cases of vulval affections.²

The coloured plates are excellent, and the sections devoted to pathology contain the results of recent research and knowledge. Possibly one of the most valuable parts of the book to the general practitioner is the frequent stressing of the effect on the skin of the vulva of substances in common use in modern times, such as liquid paraffin taken by mouth and leaking through the anus with accompanying alkaline secretion, also phenolphthalein used for the same purpose in many proprietary pills and aperient mixtures, badly made soaps, sanitary pads which on becoming moist are often alkaline, scents and powders with irritating scents, certain antiseptics and contraceptives. In this field, as in general medicine, careful history taking repays in good clinical results.

The whole field of diseases of the vulva is covered, including apart from common skin ailments malignant and benign neoplasms, microbial infections, parasitic infections and diseases due to filter-passing viruses, such as warts, herpes and *molluscum contagiosum*.

The chapter on pruritus is particularly valuable, as also is one on affections in children. In discussing estrin therapy the author draws attention to the possible dangers of prolonged or excessively large doses of estrin in such conditions as kraurosis, since it is now fully established experimentally that the prolonged administration of oestrogens can cause mammary cancer in laboratory animals.

This book should be a useful and interesting addition to the practitioner's library.

¹ "Synopsis of Obstetrics and Gynæcology", by A. W. Bourne, M.A., M.B., B.Ch., F.R.C.S., F.R.C.O.G.; Eighth Edition; 1941. Bristol: John Wright and Sons Limited. Crown 8vo, pp. 498, with diagrams. Price: 15s. net.

² "Diseases Affecting the Vulva", by Elizabeth Hunt, B.A., M.D., Ch.B.; 1940. London: Henry Kimpton. Medium 8vo, pp. 215, with 36 illustrations and 13 plates in colour. Price: 21s. net.

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CORSETS.

For many people who care to think about them, corsets have a double interest. On the one hand there is the historical side, and this is related to the æsthetic, or perhaps better, unæsthetic, compression or distortion of the female human body, practised in different parts of the world in ancient and in modern days by primitive and by so-called civilized people. On the other hand there is the practical or utilitarian side; this has not such a wide application as many people may think; but it is of importance to the medical profession because corsets can be useful and even essential in the physical treatment of certain conditions and in convalescence from others. Naturally it is the last-mentioned aspect that we wish to emphasize. The subject has recently been given prominence by an article written by Frank R. Ober, of Boston, and published by the authority of the Council on Physical Therapy of the American Medical Association.¹ To consider the surgical aspect alone would possibly be somewhat dull; it would certainly be incomplete. If a short general and historical view is taken of the subject we can understand to a certain extent the corset habits of women; but we can also see how those habits have given to medicine a useful agent in physical treatment.

History and the study of anthropology show that in many lands devices of all kinds have been adopted for the beautification of women. These devices have been dictated by custom or fashion, and have often brought much suffering on the women; sometimes the woman has been a willing sufferer and sometimes the beautification has been forced upon her. Today artificial methods are still used. Ploss and Bartels in their classical work "Woman" write: "Everywhere vanity and approbateness are ready to inflict or bear suffering in order to be beautiful. And between primitive races and fashionable ladies there is mainly this difference: that the deforma-

tions and mutilations practised by the 'savages' have the sanction of centuries of custom and tradition, whereas the others vary and change at the dictates of caprice and commerce." In many races the bodies of women are painted, tattooed and scarified; sometimes these decorations are completed with certain ceremonial rites. Modern women—the "fashionable ladies"—may or may not have secret ceremonial rites for their æsthetic adventures; but no one can deny that the cult of the "aids to beauty" is very often overdone. In the "Song of Solomon" we read that "Thine head upon thee is like Carmel, and the hair of thine head like purple". Solomon must have had a vision of some of the present-day freaks. The long finger nails of the up-to-date modern woman are a reversion to a primitive type, and the deep red lacquer that covers them completely has been described by a recent writer as typifying the blood of their victims and as an indication of their feline origin. Among certain races the cranium is deliberately deformed; but this deformation is generally applied to infants of both sexes. Ears are often pierced and heavy weights in the form of ear rings are applied so that considerable mutilation of the lobe results. It is not so long since every "civilized" woman had her ear pierced for the reception of ear rings. The binding of the feet of Chinese women that was generally practised until a few years ago is described by Ploss and Bartels as a form of beauty culture in the strictest sense of the word. When we come to the torso, which interests us most in the present discussion, we find that slimmness is and has been the admiration of many races and peoples. However, in certain parts of the world extreme plumpness of women is admired and sought. This is true of the followers of Islam. Extreme obesity is found among Tunisian Jewesses, and Ploss and Bartels remark that among the Hindus extreme plumpness has been admired since the days of Manu, who recommended his faithful to seek brides "graceful in gait as young elephants". Elsewhere slimmness is much esteemed and praised by poets and writers. Ploss and Bartels give many examples, and one or two may be quoted. From the Sanskrit come the following words of Dāmodaragupta: "Her face is almond-eyed and luminous as autumn moons: her arms slide softly from her shoulders, her ribs are narrow but carry closely set prominent breasts; her flanks are smooth and as though polished, her waist may be clasped by two hands, her loins have large buttocks and her feet curved toes." A poet of old Arabia sang: "The long tresses that adorn her are black as coals, thick and closely twisted as palm fronds. I took hold of the locks of her hair and she bent towards me; her body was slender, her hips wide and full. Her leg was like a palm stem by a fountain." A quotation from a Chinese tale, "The Casquet of Gems", reads: "Her form was slender and delicate from head to toes . . . Her waist was like a lily stem, her lips the peaches that flower round the purity of a lofty mansion walled in white." The ideal of the Japanese race is stated to have among other beauties: "A rounded throat and well-developed but not too plump figure with moderately rounded breasts. Slender hips and small, but not too thin hands and feet." The Sinhalese ideal has "breasts conical and firm as coconuts and a waist almost slender enough for a hand to span".

This brings us to corsets and the way in which they have been used and abused. A corset was first part of

¹ The Journal of the American Medical Association, April 26, 1941.

male armour; it is generally spoken of as a corselet and was a tight-fitting plate covering the torso and not the limbs. When corsets were first worn by women they were no doubt worn as a support to the figure; but the idea of armour must have clung to them, for in *The Times* of June 24, 1795, it was stated that "corsettes about six inches long and only a slight buffon tucker of two inches high are now the only defensive paraphernalia of our fashionable belles". In this connexion it is interesting to refer to the *Khalynkarts*, described by Bernhard A. Bauer as harness and clasped by him with the corset. This is a leather cuirass in which among some of the Caucasian peoples, such as the Osseties, the girl at the age of seven is literally sewn up; it encloses the breast and abdomen from the clavicle to the pelvis and has hard pieces of timber strongly bound together on a cord along the breast and down the whole length of the back. This piece of armour must not be removed day or night until marriage, when it is the husband's privilege to cut the strings. This external sign of virginity brings about atrophy of the breasts. Among what are known as civilized people the corset has for many years been worn for æsthetic reasons. Fortunately it is no longer the fashion for women to cultivate the wasp-like waists that were so common half a century ago, when the ribs were permanently deformed and viscera were displaced. Anatomical museums hold specimens of deformed ribs that were encased in this fashionable garment of torture, and the unwieldy garment itself, with its rigid supports and its elaborate lacing apparatus, is no longer flamboyant in every female patient's bedroom. To embark on a detailed discussion on the wearing of corsets in this enlightened age would be foolhardy. Certain statements can, however, be made. Everyone will admit that for some types of body build some form of correction is needed, both for the comfort of the wearer and for the sake of comeliness. Apart from this it cannot be insisted too strongly that the movements of the body should be unrestricted by any deforming apparatus. Growing girls should never be given any garment that will alter the natural shape of the body—there is all the difference between a non-constricting suspender belt and a shaped corset, even if it is made of "two-way stretching" elastic. A male observer will, of course, be told that a woman must have some "foundation garment" that will make the fall of the frock graceful, and we shall all agree that though the cleft of the nates be emphasized by a swimming costume, it should not be obvious in the ballroom. The modern *corsetière* can arrange this and at the same time can see to it that the body is not constricted or its movements impeded. These are days when physical culture and physical training are being more and more emphasized, when the muscles in young bodies are being developed in games and planned exercises, when the culture of the body is being sought. Any artificial interference with or constriction of the body will be to its detriment. Perhaps a word of warning may not be out of place. The present usage of corsets is comparatively sensible, and it is unlikely that woman will ever be willing to revert to the wasp-like waists of unhallowed memory. But woman's nature has not changed. The capricious goddess of fashion may yet decree that certain curves of the body be emphasized at the expense of freedom of movement. Many will be ready to fall into

line; but all sensible women and their doctors must combine to resist such a movement by every available means.

What of surgical corsets? In general we may say that the good features and the latent possibilities of what we may call the domestic corset, have been turned to good account by the maker of the surgical garment. Surgical corsets are designed to give support to weakened muscles or joints, occasionally almost to the stage of compression, and also to restrict movement that would be harmful or produce pain. The article by Ober to which reference has already been made, deals with corsets and backache. It has been written to bring up to date an article published in 1910 by Reynolds and Lovett, which they called "An Experimental Study of Certain Phases of Chronic Backache". These observers classified corsets as bad, neutral and good. Ober states that neutral and bad corsets are still being manufactured and sold, and he adds that the fundamental principles of Reynolds and Lovett are as true today as they were thirty years ago. They found that neutral corsets were most often worn. Bad corsets could produce chronic backache, and they had three common characteristics: (a) They were too long behind and too short in front. (b) They were cut to exert the greatest pressure at the top and bottom behind and at the waist line in front. (c) The sacral curves were strongly marked, but otherwise they did not follow the rest of the anatomy of the back. Good corsets were described as follows: (a) They were short behind and long in front, especially at the bottom. (b) They fitted snugly round the pelvis, especially between the iliac crests and the trochanters. (c) They were "incurred" at the waist line at the back and showed no curve in front. Ober compares the job of the *corsetière* with that of a sailmaker; there is an art in both. The functions of corsets, he points out, are to restrict motion, to afford protection and to restore balance. Any corset which does not do these three things will, in his opinion, not do much towards the relief of backache. He gives a long list of essential requirements for the application of corsets; these should be studied by anyone specially interested in the subject. Perhaps it should be pointed out that what is described as the most important feature of any corset is the way in which it fits over the iliac crests. "The cloth of this part of the corset must be so cut that the crest of the ilium fits into a sort of pocket." A great deal that Ober writes about corsets and backache will be applicable to these garments when they are made for other purposes, such as the support of the weakened abdominal wall after surgical operation. Two of his contentions are of such importance that they may be used to close the present discussion. The first is that the work of the medical attendant is not finished when he has turned the patient over to the corset maker. He should not only give exact directions regarding the type of support that is needed, but he should inspect the completed article and should superintend any alterations that may be necessary. Finally, when the symptoms for which the corset was ordered have disappeared, measures must be taken to restore the tone of the patient's muscles so that the use of the garment may be discontinued. Thus we conclude that man or woman, sick or well, should cultivate the body muscles so that they may fulfil their functions without any artificial aid.

Current Comment.

DYSPEPSIA.

THE late Lauder Brunton, writing in Allbutt and Rolleston's "System of Medicine" in 1907, stated that dyspepsia was a general name which was generally used as synonymous with indigestion. The word comes from the Greek *δυσ*, a prefix meaning bad or difficult, and *πέψω*, to digest. Brunton pointed out that its significance was vague, but he held that its vagueness had both advantages and disadvantages. The disadvantages of the name were that it signified so many different conditions that it was little or no guide to the exact functional or organic lesions of the several organs concerned in the digestive process. Its advantages were that it included a group of symptoms which could not always be referred to an exact physiological or anatomical basis. Brunton thought that as medical knowledge advanced the use of the name dyspepsia would be greatly restricted and it would be possible to assign the different forms of indigestion more and more exactly to their proper causes. Since Brunton wrote these words medical knowledge has advanced; chemical, radiological and endoscopic methods of examination have been made available; and some conditions formerly but dimly recognized can now be labelled and as it were pigeon-holed. But in spite of all this, the terms "indigestion" and "dyspepsia" are still very useful, partly on account of the convenience associated with their use and partly because of the gaps still remaining in our knowledge. This has recently been emphasized by T. Grier Miller, Professor of Clinical Medicine in the University of Pennsylvania School of Medicine.¹ Miller states that no more satisfactory term than dyspepsia or indigestion (he prefers indigestion) has been devised to indicate a syndrome that includes a subjective sensation of epigastric discomfort or pain, often related to meals, anorexia, gaseous eructations, regurgitations, nausea and vomiting, and sometimes headache, palpitations and general nervousness and weakness. The justification for recognizing the syndrome is, in Miller's opinion, not that it constitutes a diagnosis, "for after all it is no more a diagnosis than hypertension, dyspnoea or jaundice is". Just as each of the terms hypertension, dyspnoea or jaundice connotes a group of clinical phenomena, explainable on the basis of a disturbed function of the body, so indigestion "designates a picture of disturbed gastric physiology". The dysfunction is itself a manifestation of some more fundamental disorder of the body. This is the point of view of a professor of clinical medicine. Dyspepsia is usually looked on as a medical rather than a surgical condition, and is as a rule approached from a physician's standpoint. It has been considered recently by a surgeon in a somewhat unusual way that should be brought to the notice of readers of this journal.

During recent years it has been recognized more and more that medicine and surgery cannot be shut off from one another in separate closed compartments. The surgeon particularly is approaching his problems more and more from the point of view usually conceded to the physician; he thinks more than he did in terms of physiology, and he realizes that his altered attitude is giving him added power. In his important and notable work "The Surgery of the Alimentary Tract", Sir Hugh Devine, of Melbourne, has dealt with upper abdominal conditions in terms of dyspepsia. The approach is original and also practical; it should be studied not only by the surgeon, who cannot fail to benefit from the views expressed, but also by the physician and general practitioner. After all, it is the physician and the general practitioner who usually see the patient first; they have to recognize the indications for surgical measures when they arise, and in this they will be helped by what Devine has written. The surgeon will probably seek the book for the technical advice that the author is so well qualified to give, but he will find in addition a mental

stimulus that will be the greater because it will be of a kind that is probably unexpected.

Devine describes dyspepsia as an awareness of the process of digestion. It is caused, he states, by a great variety of diseases—its main cause is disease of the stomach, but it may arise from disease anywhere in the alimentary canal or "as a reflexion of disease in any part of the body". His words are very like those of Miller, already quoted, and show how urgent the matter of diagnosis of the fundamental cause really is. In the preface of his book Devine admits that he has devoted the first part to the diagnosis of dyspepsia because in his own abdominal surgery the weakness has been "incompetence in clinical diagnosis in contrast to increasing competence in radiological diagnosis and surgical treatment". This is an admission that many surgeons, and for that matter clinicians of other types, would make if they were really honest with themselves. We might apply to proficiency in diagnosis a remark once made by the late W. A. Holman, sometime Premier of New South Wales, who said to a friend that if one did not know a great deal about a subject the best way to make good the deficiency was to write a book about it. We do not suggest that all medical folk who wish to perfect their diagnostic ability should write books; we should plead for mercy if they did. Failing this, however, they can benefit from the book that a discerning clinician, honest with himself, has written for them.

One of Devine's main objects has been to make easier the recognition of syndromes of dyspepsia that are not like those commonly described in text-books. He has described what he calls "patterns" of dyspepsia, which are the manifestations of early disease and which can be learned only from study of the pathological changes in living tissue at the operation table and from review of the case history in the light of findings at operation. Each of these patterns may indicate either a particular phase of functional disturbance of the stomach or a type or a degree of organic disease of the stomach. Examples are given. Functional disease of the stomach may cause a dyspeptic syndrome almost indistinguishable from that of early carcinoma; it may, on the other hand, produce a clinical picture of dyspepsia which is easily confused with that caused by a type of gastric ulcer. Again, a certain type of carcinoma of the stomach may give rise to a dyspepsia similar to that of gastric ulcer, and another type may cause a dyspeptic picture similar to that found in duodenal ulcer. Further, an extragastric alimentary lesion may cause a dyspepsia like that of gastric ulcer or carcinoma, and systemic disease may give a picture of organic disease of the stomach. Devine, of course, is writing particularly for surgeons, and he discusses the surgeon's approach to the problem of diagnosis in a case "which may have a surgical cause". His words will apply equally well to any practitioner in similar case. The practitioner may approach the problem from the standpoint of a knowledge of how the physiological conditions of the stomach are disturbed, and he may try to analyse the dyspeptic picture—he may inquire into the mechanism of its causation. On the other hand, he may approach the problem from the etiological point of view—from his knowledge of the phases of disease which he knows produce dyspeptic syndromes. In discussing the functions of the stomach, Devine lays stress on the motor function—"the main function of the stomach is its motor activity, that is, its filling and its emptying". Miller holds similar views on the importance of the motor function. He states that the clinical manifestations of indigestion are probably always immediately dependent on a disturbance of the motor function of the stomach and rarely of the secretory function. Secretory alterations are believed to be important, Miller adds, chiefly because of their effects on the motor function of the stomach. Devine thinks that the secretory function of the stomach is affected chiefly by toxic, circulatory and nervous disturbances and that the dyspepsia thus caused is a painless dyspepsia. Generally speaking, the motor function is affected more by organic disease and is a painful dyspepsia. To these general statements there are of course exceptions.

¹ The New England Journal of Medicine, March 27, 1941.

To understand the varying clinical manifestations associated with disturbance of the motor function it is necessary to know how gastric pain can be produced. This, Devine states, involves a consideration of the following: (a) the sensory innervation of the stomach; (b) the nature of the postural gastric tone underlying gastric retention, that is, the mechanism concerned with the filling of the stomach; (c) the nature of the gastric postural tone underlying the expulsive action of the stomach, that is, the mechanism concerned with its emptying; (d) the mechanical effects of the various degrees and stages of organic diseases.

Turning to the aetiological point of view, Devine divides dyspepsia into four groups: (a) dyspepsia caused by disturbance of the vitality of the gastric or duodenal wall, the result of local or systemic disease, "vitality dyspepsia"; (b) dyspepsia arising as a result of a disturbance of the neuro-muscular function of the stomach, "functional dyspepsia"; (c) dyspepsia occurring as the result of neuro-muscular disturbances either in other parts of the alimentary canal or in its adnexal organs, such as the appendix, gall-bladder or pancreas, "reflex dyspepsia"; (d) dyspepsia caused by organic disease of the oesophagus, stomach or duodenum, "organic dyspepsia".

We do not propose to attempt the description of any of the patterns discussed in detail by Devine. He has separate chapters on the dyspepsia of acute gastric ulcer, of uncomplicated chronic gastric ulcer, of complicated gastric ulcer, of acute duodenal ulcer, of duodenal diverticulum, of jejunal ulcer, of benign and other tumours of the stomach, and carcinoma of the stomach and duodenum. Devine states that the surgeon should approach the diagnosis of cases of dyspepsia "from the point of view of cultivating the art of recognizing the pattern of a dyspepsia by a knowledge of the mechanism of its causation". The general practitioner can try to do this with dyspepsia of all kinds. Those who have the opportunity of studying Devine's book will find some of the patterns dealt with in the chapters that have been enumerated full of useful information. Perhaps the most valuable feature in Devine's method of dealing with the subject is his insistence on an inquiry into causation and into the mechanism underlying clinical conditions. In accordance with the assiduity and the intelligence displayed by the clinician in his investigations will his mental patterns, his conception, of the many forms of dyspepsia be made clear. Lauder Brunton in the early days of this century pleaded for accuracy of diagnosis and terminology; this need is still with us, but we need not seek to discard the term; what we need to do is to allow our use of it to be a measure of our intelligence and not of our ignorance.

THE TREATMENT OF HYPERTROPHIC PYLORIC STENOSIS.

HYPERTROPHIC pyloric stenosis of infants is a disease that can be treated either medically or surgically, and each method has its ardent followers. When Ramstedt in 1912 introduced his muscle-splitting operation, the value of this procedure was quickly realized, and for many years now it has been the only operation used for the disease. Almost as important as the operation is the careful nursing and feeding of the infant during the ensuing days. Breast milk is unquestionably the best food, and the infant can usually be put to the breast the day after operation. Before 1912 medical treatment was given a thorough trial in almost all cases before resort was had to surgery. At that time it consisted chiefly of repeated gastric lavage and frequent small feedings, the food sometimes being thickened. The first important advance in medical treatment came with the use of atropine, given before feedings, with the apparent result that the contracted pyloric sphincter was relaxed. The next and most important advance was the introduction of eumydrin, which is atropine methylnitrate. It is said to be fifty times less poisonous than atropine, though the effective antispasmodic dose is only two or three times larger. It was introduced in Denmark and its use in a series of cases

was first described by E. Svensgaard¹ in 1935. She gave each day seven doses, each consisting of five mls of a 1 in 10,000 solution, and each being given about half an hour before a feeding. Experience has shown that the drug given in this way is sometimes vomited before absorption can have occurred, and recently A. Wallgren has described the lingual administration of a more concentrated alcoholic solution. A 0.6% solution in alcohol is used, and doses of one or two drops are placed on the tongue, whence the drug is rapidly absorbed.

At the present time, then, there are two popular methods of treating pyloric stenosis; one is surgical by Ramstedt's operation, the second is medical by eumydrin. From examination of published reports it is exceedingly difficult to make a satisfactory comparison of the two methods; but there is little doubt that the mortality is less when medical treatment is used. A somewhat incomplete but fairly representative survey of the literature of recent years reveals that among approximately 1,000 children treated medically there was a mortality rate of 6%. Many of the children did not have eumydrin, and the mortality rates with this drug have varied from 1% to 12.5%. Surgical treatment, however, has been used in recent years in about 3,000 published cases, with a mortality rate of approximately 14%. Some surgeons with large series have a mortality rate as low as 3%; one large German clinic obtained a mortality rate of 18.4% with medical treatment and only 3.4% with surgical treatment. There have been no recent reports of large series from Australian hospitals, but the annual reports of the Royal Alexandra Hospital for Children, Sydney, where surgical treatment exclusively is used, reveal that in the last ten years 302 affected children have been treated with a mortality rate of 6.9%, figures which compare favourably with those of most surgical institutions. The subject of death rates in this disease cannot be left without mention of the surprisingly bad results reported in England. Helen Mackay² has recently reviewed some of them. She lost five of forty patients treated medically. The death rate of all reported cases in England treated with eumydrin is 11.5%, and in series treated surgically commonly ranges between 13% and 25%. In the Hospital for Sick Children, Great Ormond Street, the year's mortality rate has never dropped below 21%.

Before a hasty conclusion is stated that any one method of treatment is superior, these reports must be considered more critically. There are certain important factors that help determine the results. The first is the criteria of diagnosis. In surgically treated cases the diagnosis is always checked by actual inspection and palpation of the pyloric tumour at operation. When medical treatment is adopted diagnosis rests on the vomiting, gastric peristaltic waves, constipation, and, most writers insist, palpation of the pyloric tumour. This palpation is an exceedingly difficult procedure and often requires much skill and patience. It is never as convincing as the finding of the tumour at operation, and it is quite possible that among medically treated patients there are actually some who are suffering from pylorospasm, the cure of which is usually easy enough. The second factor is the time that has elapsed between the onset of symptoms and diagnosis, and the condition of the child when treatment is commenced. It is impossible to compare the importance of this factor in different series. There is no doubt at all that the better the condition of the child before treatment, the better the prognosis, particularly if the treatment is surgical. When a total is made of a number of series from several countries it is unlikely that this factor is of much importance in the determination of the different results obtained by surgical or medical means. It may, however, help to account for the bad results in a single country. It is important, too, to consider the actual causes of death. Among these, and an ever-present danger, is the risk of alimentary or respiratory infections during treatment. This is always a problem in paediatric hospitals, and in England, on Mackay's admission, accounts for many deaths. In Continental reports it does not often

¹ Archives of Disease in Childhood, December, 1935.

² Archives of Disease in Childhood, March, 1941.

occur, nor is it common in Sydney. If there were something wrong with the nursing or hospital control in England, this would be a large factor in causing the unsatisfactory results reported. Some deaths are purely surgical, and result from shock or from wound infection with rupture of the abdominal wall or peritonitis, and surgical deaths generally take place among the patients whose condition is poor before operation; whether any different result would have been achieved in these cases by medical treatment it is almost impossible to say. The remaining deaths are from marasmus among patients who do not respond to treatment. If the operation is properly performed, most of these come in the group treated by medical means. A final factor determining the outcome of treatment is the skill of the surgeon, anaesthetist, physician and nursing staff, another factor that cannot be compared from series to series.

While, therefore, reported results do suggest that medical treatment is superior to surgical, it is impossible to be certain of this, for no faultless comparison is yet possible. The method used will depend largely on the facilities available and conditions prevailing. Surgical treatment is of considerably shorter duration, but the child must of necessity be in hospital. A skilful and experienced surgeon, anaesthetist and nursing staff are essential. Medical treatment is longer, but in mild cases can be carried out at home if the hospital available is plagued by much cross-infection. In the more severe cases among patients who must be in hospital for many weeks, such cross-infection may influence the choice of the quicker surgical method. At present it is probably wise for any hospital that is achieving good results to retain the method it knows and uses with success; but if surgery is producing bad results a change might well be indicated. Useful findings might follow an attempt to determine whether some types of case are specially suited for medical and some for surgical treatment; from published results this cannot be decided.

THE DIAGNOSIS OF HYPOTHYROIDISM IN CHILDHOOD.

It is a simple matter to diagnose cretinism in a child when it is sufficiently pronounced and when enough time has elapsed for obvious structural abnormalities to have developed. It is very much more difficult to make the diagnosis in the mild and early cases, in which therapy is most likely to be successful. There is a temptation, too, for physicians to make the diagnosis uncritically in the examination of abnormal children, because they may be lured on by the knowledge that in thyreoid extract they have an effective medication if only the diagnosis is right. "If a child's eyes are widely spaced or his nose is flat or if he is mentally retarded or physically stunted, he may be diagnosed as a cretin. In fact, almost any infant who is retarded in development or who is peculiar or ugly runs the chance of being branded as having hypothyroidism." These words are taken from a recent article by L. Wilkins and W. Fleischmann,¹ who have been specially interested in cretinism for a number of years, and have in the last few months contributed several articles on the subject.² These workers emphasize two new and very interesting aspects of the subject.

The manifestations of hypothyroidism in childhood fall into two main groups, the functional and the structural. The former are present and more or less obvious from the onset of the complaint. The latter of course take time to develop and depend on the duration and age of onset of the disease. The functional changes are physical and mental torpor, impaired peripheral circulation, constipation, certain pulse changes and biochemical and metabolic changes. The torpor may be so obvious that the parent complains of it. Often, however, the parent with misdirected pride says the child is "very good and never cries". The skin is pale and cool and may appear to be slightly

tinged a yellowish colour by carotene or a greyish colour. Sweating may be normal or decreased. The pulse is slow and the pulse pressure diminished, though this can seldom be accurately determined. The basal metabolic rate is low, but its estimation in children is too unreliable to be worth while. Obese children without hypothyroidism may show a low rate, and this one laboratory finding in a child most emphatically does not justify the diagnosis of thyreoid deficiency. The blood cholesterol varies from quite low to abnormally high figures in these children and is of no diagnostic value. Wilkins and Fleischmann, together with W. Block, however, found significant changes after thyreoid medication. During treatment with thyreoid the blood cholesterol tends to fall, and after treatment is stopped rises to abnormally high levels. These changes do not occur in normal children. Another valuable biochemical test described by these workers depends on creatine excretion. The excretion in the hypothyreoid or normal child varies considerably from day to day and is of no value in the diagnosis of thyreoid deficiency. If, however, the normal child is given either thyreoid extract or thyreotropic hormone, there results an increase in creatine output. The hypothyreoid child shows this increase in response to thyreoid but not to thyreotropic hormone, for his thyreoid gland is incapable of responding to pituitary stimulation. Some normal children are found to respond to neither of these preparations, a result called by Wilkins and his colleagues the "false negative response". These two biochemical tests, though rather elaborate, appear from Wilkins's results to be of real value in substantiating the diagnosis of thyreoid deficiency in the many children whose physical or mental status makes the condition suspect but not obvious.

The structural changes of hypothyroidism do not become apparent until the condition has been present for some time. They include dwarfing, facial changes, retardation of ossification and dental development, and cerebral degeneration. Often, but not always, the skin is dry, the hair coarse, and the soft tissues, including both tongue and subcutaneous tissue, increased in size. The decrease in height is due chiefly to shortness of the lower limbs. In normal infants the symphysis-sole length is distinctly less than the symphysis-vertex length. At the age of about ten years these measurements become equal. In cretins the infantile proportions persist. Most other dwarfs, unless achondroplasia is the cause, show normal skeletal proportions. The facial abnormality, which consists of a short undeveloped nose with a wide bridge, is again an infantile configuration. The osseous retardation can be displayed by radiological examination of the limbs, particularly the wrist, or in infants the knee, but is not an infallible sign of thyreoid deficiency. Of more interest is an irregularity of ossification that has been described by Wilkins.³ The change is best seen in the head of the femur and the tarsal navicular. There is first a delay in calcium deposition. When, however, it does occur it starts not in a single centre which spreads uniformly peripherally, but in a number of small spots, which gradually enlarge and coalesce and increase irregularly. They give a fluffy, stippled or fragmented appearance to the developing epiphysis, which in the femur may even be confused with Perthes's disease. The authors publish some interesting and convincing X-ray photographs. This irregular ossification has previously received little attention. It may only be found, of course, if serial X-ray photographs are made in a suspected case, for eventually the epiphysis becomes completely ossified even in the cretin.

The work of Wilkins, Fleischmann and Block merits attention, not only because they have made a comprehensive survey of a difficult subject, but because of their two new contributions. These are the tests of the biochemical response to thyreoid medication as measured by creatine excretion and blood cholesterol, and the mode of ossification of certain epiphyses in hypothyroidism. In the frank example of the disease the diagnosis will still be made on clinical grounds alone, but in difficult and doubtful cases these tests may well be used.

¹ *The Journal of the American Medical Association*, May 31, 1941.

² *The American Journal of Diseases of Children*, January, 1941.

Abstracts from Medical Literature.

GYNAECOLOGY.

Endometrial Cyst and Endometriosis.

ALEXANDER A. LEVI (*The New England Journal of Medicine*, January 23, 1941) reports the case of a thirty-nine year old woman who had a pedunculated endometrial cyst of the uterus and endometriosis of the uterine wall. Both of these conditions, he states, are rare. The patient had also an intramural fibroid and a dermoid cyst of the left ovary. The author quotes Crile's definition of endometriosis and also his suggestion that there may be an underlying endocrine factor in its aetiology, as fibroids of the uterus, endometriosis and menorrhagia are often associated.

The Action of Drugs on the Human Uterus.

J. A. GUNN (*Edinburgh Medical Journal*, May, 1941) remarks that both in laboratory work and in clinical practice undue and unnecessary reliance is often placed upon instrumental methods. The value and difficulties of simple observation tend to be underestimated. The author considers the action of ergot, pituitary extract, quinine, adrenaline and morphine on the human uterus. Original work on the effect of these drugs on excised strips of uterine muscle is included. Chassar Moir's work on the active principles of ergot is outlined. This was the first occasion on which an important discovery had originated through mechanical recording of the contractions of the human uterus itself. The responses of uterine muscle to chemical agents may depend upon the stage of the sexual cycle or upon previous influence of sex hormones, and due cognisance must be taken of this. Pitocin acts especially on the pregnant uterus, which becomes more sensitive to the action towards the end of pregnancy. Pitressin acts mainly on the non-pregnant uterus. In some animals quinine has a very powerful stimulating action. In the human being the action is not nearly so powerful and there is great uncertainty as to its value. With adrenaline, Bourne and Burn produced a brief relaxation of the human uterus *in situ*. In higher concentrations with excised strips of uterus the author produced stimulation. With ether, the intervals between the contractions are prolonged and their intensity is decreased as anaesthesia deepens. Clinical experience and graphic methods both suggest that the action of morphine on the contractions of the parturient uterus is not constant.

Menometrorrhagia.

E. HENRIKSEN (*American Journal of Obstetrics and Gynecology*, February, 1941) has reviewed 1,500 patients between the ages of twenty and forty years who were suffering from abnormal bleeding. He states that in spite of our knowledge of the activities of the female genital tract, the fundamental causes of either normal or abnormal bleeding are still not fully understood; the advent of organotherapy has led to its use without proper investigation to such an extent that the author considers that the term functional bleeding is much

abused. The treatment of the symptoms of abnormal uterine bleeding is frequently carried out without rhyme or reason, and consists mostly of injections into the buttock of various minerals and endocrines. In a proportion of the patients an inflammatory reaction was found to have spread from the cervix to the lower uterine cavity. In regard to the ovary the author found that it often became enlarged after operation, but returned to normal within a few months. In spite of reports as to the importance of the uterus in relation to the ovary, the author believes that if the tissue of the ovary at the time of hysterectomy reveals normally functioning follicular elements the function will continue to be normal after the removal of the uterus. This is based on the clinical findings in these patients following surgery.

Fracture of the Femoral Neck following X-Ray Therapy for Gynaecological Malignant Disease.

H. STRAUSS AND J. L. MCGOLDRICK (*American Journal of Obstetrics and Gynecology*, June, 1941) report three cases of their own and review the literature on fracture of the femoral neck following X-ray therapy. Excluding pathological fracture due to metastases, the evidence is becoming more conclusive that some fractures may be directly attributed to the radiation effects on the normal bone and its vascular supply. It is the authors' opinion that the small increase of depth dose with treatment through lateral ports does not justify the added risk, and it must be borne in mind that the vascular supply of the femoral neck is terminal and is vulnerable to post-radiation vascular occlusion. The authors conclude that though it is justifiable to use palliative therapy, the clinician must keep in mind that he is treating the patient and not the disease.

Cancer of the Cervix following Supravaginal Hysterectomy.

G. G. WARD (*American Journal of Obstetrics and Gynecology*, April, 1941) does not agree with the general impression that cancer of the stump is more serious, more difficult to treat, and with less hope of success than cancer of the cervix when the fundus is present. He analyses the records of a women's hospital from May, 1919, to May, 1940. This shows that of 879 patients 6.9% had carcinoma of the cervical stump. The survival rate for all cases was 42.8%. The author's opinion is that the total operation is to be preferred, but that in average hands there is with this operation more danger of a higher mortality and injury to bladder and ureters than in skilled hands. Even the expert surgeon in some cases will find it wiser to carry out the subtotal operation. However, in all subtotal operations the possibility of cancer of the cervix must not be overlooked.

Inhibition of Lactation.

H. L. STEWART AND J. P. PRATT (*American Journal of Obstetrics and Gynecology*, April, 1941) has investigated the question whether the inhibition of breast engorgement is synonymous with inhibition of lactation; he has also tried to determine the effect on breast secretion when stilbestrol, testosterone or theelin is administered early in the post-partum

period. If these hormones inhibit breast secretion, he wants to know whether the effect is temporary or permanent. In a study of normal lactation among 900 consecutive nursing mothers it was observed that breast engorgement does not consistently indicate the amount of subsequent milk production. The authors have come to the conclusion that the inhibition of breast engorgement is not synonymous with the inhibition of breast lactation. The engorgement of the breasts may be prevented by suitable doses of stilbestrol, 15 to 35 milligrammes; and lactation may be diminished temporarily by stilbestrol, but the individual response varies widely. They found that the effect on lactation of 250,000 international units of theelin and 125 milligrammes of testosterone was negligible.

OBSTETRICS.

Fœtal Respiration.

F. F. SNYDER (*American Journal of Obstetrics and Gynecology*, February, 1941) has investigated the respiratory movements in fetuses in the amniotic sac. The amniotic fluid was coloured by a 50% indian ink solution. It was noted that of the 30 fetuses examined, 17 breathed and 13 were apnoeic. In those who breathed, the particles of ink were regularly observed in the lungs, whilst it was absent in those who were apnoeic. It is suggested that the present findings provide a new link in the chain of evidence by which intrauterine pneumonia is connected with abnormality of the amniotic fluid.

W. F. WINDLE criticizes Snyder's article and points out that the reason why some fetuses made respiratory movements *in utero* and others did not depended on the extent to which the respiratory centre was stimulated by lack of oxygen. His experiments have led him to believe that aspiration of amniotic fluid is not a normal action.

The Prognosis for the Fetus in the Toxæmias of Late Pregnancy.

F. J. BROWNE AND GLADYS H. DODDS (*The Journal of Obstetrics and Gynecology of the British Empire*, October, 1940) attempt to estimate the prognosis for the fetus in the toxæmias of late pregnancy. They use their former classification of preeclamptic toxæmia, eclampsia, essential hypertension complicating pregnancy, chronic nephritis complicating pregnancy, and recurrent toxæmia. The salvage of live infants is taken as the number of infants discharged alive from hospital compared with the number of births. In preeclamptic toxæmia the salvage of live infants was 87%, in eclampsia 52%, in chronic hypertension 62%, in chronic glomerular nephritis 63%, and in recurrent toxæmia 80%. The authors consider that with more recent methods of diagnosis the salvage of live infants should be 75%.

The Magnesium Sulphate and Ether Circulation Times during Pregnancy.

M. BERNSTEIN AND S. SIMKINS (*American Journal of Obstetrics and Gynecology*, June, 1941) have made an investigation on the blood velocity during pregnancy in 300 patients. Their technique was to inject five cubic centimetres of a warm 10% aqueous

solution of magnesium sulphate into the antecubital vein. With the arm at the level of the left auricle the time is noted when the patient reports a sensation of heat in the tongue and pharynx. This test was followed in about one minute by the ether test, which is carried out by injecting five minims of ether and five minims of warm normal saline solution. The patient usually coughs and records the presence of ether by a grimace. The average ante-partum time was 9.9 seconds and post-partum 10.4 seconds. There was, however, a fair degree of individual variation. The authors concluded that the circulation time showed that there was a speeding up of the circulation time in pregnancy, except in the presence of cardiac involvement, when the time was unduly prolonged.

The Human Corpus Luteum of Pregnancy.

JOSEPH GILLMAN AND H. B. STEIN (*Surgery, Gynecology and Obstetrics*, February, 1941) have studied *corpora lutea* from normal cases of intrauterine pregnancy. They point out the importance of examining only fresh material, as lipid and colloid rapidly disappear after death or removal from the body. The *corpus luteum* increases rapidly in size after the fiftieth day of pregnancy. Owing to a gradual obliteration of the central cavity and a diminution in the thickness of the surrounding fibrous tissue, it diminishes in size after the sixtieth day. The amount of lutein tissue remains constant throughout pregnancy. The central cavity contains a potent hormonal fluid. The theca-lutein cells reach their greatest development at the second to third month. They disappear shortly after the obliteration of the central cavity. The granulosa-lutein cells persist throughout pregnancy. Both types of cells contain secretory granules, lipid and chromidial substance. The granulosa-lutein cells also contain vacuoles and colloid droplets. The authors suggest that involution of the *corpus luteum* of pregnancy may have commenced as early as the second month. They regard the fiftieth to the sixtieth day of pregnancy as the critical period. At this time the *corpus luteum* undergoes remarkable structural changes. These changes parallel the metabolic changes shown in the urinary excretion of pregnandiol, gonadotropic substances, and the oestrogens.

Toxæmia of Pregnancy.

CHARLOTTE A. JONES (*American Journal of Obstetrics and Gynecology*, February, 1941) realizes that the term "toxæmia of pregnancy" denotes a "diagnostic trash can", but uses it for the want of a better term and in the belief that this terminology will soon become obsolete in medical literature. She has made a survey of 425 cases of toxæmia of pregnancy. The histories of the patients showed that 46 had spontaneous abortions. Oedema was by far the commonest manifestation. For patients with early symptoms the régime was to add protein and carbohydrate to the diet, to give advice as to rest, to administer magnesium sulphate and to limit the use of sodium chloride. Vitamin B and iron were given as a routine measure. The series covers a ten-year period and the cases occurred amongst 7,293 deliveries. The maternal mortality rate was 0.04% and the fetal mortality rate 9.6%. In following up the patients the author has come to the conclusion that recur-

rence is more frequent than was formerly thought and that damage to the cardio-vascular renal system is often far-reaching, even in supposedly mild cases of toxæmia of pregnancy.

Objections to the Induction of Labour in Normal Pregnant Women.

EDWARD L. CORNELL (*American Journal of Obstetrics and Gynecology*, March, 1941) remarks that in the past ten years advice to induce labour on the mildest indications is increasing rapidly in the literature. Convenience of the patient or physician is at times the only indication. He refers to this as "streamlined" obstetrics. It is fallacious to predict that a patient is at term by the apparent size of the fetus, by the date of the last period or by the date of quickening. If reliance is placed on these factors, many premature babies will be delivered. The common complications of induced labour are prolapse of the cord, fetal mortality, placental infection, post-partum hæmorrhage, and rupture of the uterus. From observation and a review of a series of 200 consecutive normal pregnancies the author firmly believes that interference, either medicinal or surgical, with the natural processes of pregnancy and labour in normal women is not justified. He protests against the practice.

Inversion of the Uterus.

PROBODH DAS (*The Journal of Obstetrics and Gynecology of the British Empire*, October, 1940) states that inversion of the uterus is so rare that many medical men never see a case. The author has reviewed the literature and made a statistical study of 391 cases. The condition is more common in India than elsewhere. The frequencies of acute puerperal inversion are: India, 1 in 8,537; America, 1 in 23,127; and Britain, 1 in 27,992 in obstetric hospitals. In the authors' series 83.65% of cases were of puerperal origin; of these, 73.4% were acute. In the non-puerperal group only 8.6% were of sudden origin. The inversion is complete in 80% of the puerperal cases and 92% of the non-puerperal cases. In the non-puerperal group 78.8% occurred in patients who were between thirty-one and sixty years of age. In puerperal inversion primiparity was responsible for 52% of cases.

The Immediate Treatment of Obstetric Hæmorrhage and Shock.

CHARLES A. GORDON (*American Journal of Obstetrics and Gynecology*, June, 1941) states that puerperal mortality in the city of New York has steadily declined, yet deaths from hæmorrhage grow no less. He analyses the cause and suggests more active measures. In 1938 hæmorrhage caused 27% of the puerperal deaths; in 1939, 35%. In Brooklyn, where every obstetric death is investigated, it is found that hæmorrhage is the most controllable factor. Too little blood is given, or none at all, or perhaps it is given too late. Although it is not always possible to prevent hæmorrhage, preparations can be made to meet it and treatment can be instituted before the patient has developed grave shock. There are other factors besides actual blood loss which turn the scale against the patient, such as dehydration, long labour and anaesthesia. The increased use of the barbiturates is not to be forgotten, and where these are used extensively,

preparations must be on hand to combat shock. The use of oxygen is rational for anoxia, but cardiac stimulants are contraindicated, since shock is not of cardiac origin. Loss of plasma is responsible for the symptoms whether due to hæmorrhage or not, and it is important to realize that the danger lies less in the loss of red blood cells than in loss of blood volume. For immediate treatment crystalloids are of such temporary benefit that a colloidal substance is desirable, since solutions of acacia cannot be unreservedly recommended. The desirable agent is plasma, and the plasma bank is practicable for the smallest hospital while a blood bank is not. Those lying-in institutions without facilities for transfusion, with no microscope, and with no one able to cross-type blood, will soon have no excuse, for blood serum for emergencies is now commercially available. Obstetricians should be prepared for hæmorrhage and shock before, during and after every labour they conduct.

The Value of Calcium in Labour and in Uterine Inertia.

G. D. PATTON AND R. D. MUSSEY (*American Journal of Obstetrics and Gynecology*, June, 1941) have carried out an investigation to see whether the intravenous use of calcium would relieve the pain of labour and to determine the effect of calcium on the contractibility of the human uterus during labour. Twenty-six women were studied. Calcium gluconate was given intravenously and tracings were taken on a smoked drum. The results showed no relief from the pain of labour; in many instances pain was increased. The effect on uterine contractions was one of stimulation; in no case did tetanic spasm develop. When the patient was not in labour calcium had no effect and the authors conclude that it may be employed clinically to good advantage in uterine inertia; its duration of effect seems to be two to three hours; it is contraindicated in the presence of the digitalis group, as the two drugs acting together may bring about a ventricular standstill. Also its beneficial action is minimized by the action of "Pentobarbital sodium" and other analgesics. It has no effect on the babies. Briefly, it increases the intensity, lessens the interval, but does not lengthen the duration of the uterine contractions.

Effect of Vernix Caseosa on Bacteria.

HERBERT LUBINSKI AND BEN BENJAMIN (*The Canadian Medical Association Journal*, February, 1941) have studied the possible causative factors of pemphigus. They remark that the evaluation of the efficiency of any one or any combination of prophylactic or other forms of treatment is extremely difficult. Two papers suggesting that the excess blood should simply be wiped off the skin at birth and that the skin should then not be washed or disturbed during the stay in hospital were noted. When this method was tried by the authors, no lesions were observed for several months, but without any apparent change in procedure a number of infants developed pustules. The authors then tested *vernix caseosa* for antibacterial action. They found that vernix had no inhibitory effect on the growth of staphylococci or *Bacillus coli in vitro*. Further, it produced no inhibition of invasion through the skin and lethal intoxication by *Bacillus diphtherie* in guinea-pigs.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on June 26, 1941, at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, Dr. WILFRED VICKERS, the President, in the chair.

Pertussis Immunization.

DR. D. G. VICKERY read a paper entitled "The Value of Immunization in Pertussis" (see page 221).

DR. PHYLLIS ANDERSON said that she did not intend to speak of the value of immunization of the child population against pertussis, as she believed that it had been proved by well organized and controlled field studies in the United States of America. She wished to refer shortly to the meaning of terms which were freely used in discussions of the subject. Immunity had been briefly described as resistance to disease. The methods by which the statement had been upheld included the following: demonstrations of barrier action of surfaces against the organism itself, formation of antitoxin, stimulation of leucocytic activity and phagocytosis, and the production of antibodies possessing the ability to agglutinate the organism or to produce complement fixation in the presence of suitable antigen. The process known as immunization was really an attempt to produce in the patient some of those immunity reactions which could be brought about in laboratory animals, and so to endow the subject with increased resistance to the particular disease. The first immunization procedure, Jennerian vaccination, had given bacteriologists a perfect test, because they could reinoculate the subject with the living infective agent and demonstrate complete or partial immunity as the result of their efforts. In certain other diseases, notably diphtheria, they used a skin test to demonstrate the production of one type of immunity reaction and the presence of resistance to a dangerous result of infection with *Corynebacterium diphtherie*. Immunization against diphtheria did not prevent the organism from establishing itself in the subject; indeed, such immunized people might carry the bacillus for many months in large numbers. Vaccination with the typhoid-paratyphoid group of organisms was followed by the production of agglutinins in the subject's serum to a greater or lesser concentration; but there was ample proof that a low titre of agglutinins did not necessarily indicate absence of resistance to infection.

Dr. Anderson went on to say that in the investigation of pertussis the information gained from immunity reactions was even less definite. During the natural disease complement-fixing antibodies appeared in the serum; the same thing occurred after vaccination. One American worker had used this test to control the effect of her immunizing injections; if a complete positive reaction was not obtained, she gave further doses of vaccine, up to 14 cubic centimetres of the standard emulsion. She believed that in her small series the immunity conferred lasted about as long as that developed during an attack of the disease, if this test was used as a standard. Dr. Anderson said that in other large-scale experiments the serum reactions had not been estimated; the technical problems in experiments of this size might well make the laboratory worker pause before attempting such a task. There was some evidence that the size of the local reaction might be related to the size of the dose of vaccine injected; but Dr. Anderson knew of no facts which proved the existence of a negative phase of antibody production in pertussis vaccination. In other words, there did not appear to be a fall in the level of circulating antibodies before the rise which followed the second dose of vaccine, nor did there seem to be evidence to show that the existence of such a condition would create an increased susceptibility to infection with the organism.

Dr. Anderson further said that as yet the only reliable test of the success of immunization was the absence of symptoms of the disease after the subject had been in close contact with a person who had been proved to harbour the organism. This had been used as a standard in the American mass experiment, in which coordination between laboratory, clinical and clerical staffs had been achieved over a considerable period of time, and results had been judged wholly on the resistance exhibited by vaccinated and control children who had been exposed to proved contact with *Hæmophilus pertussis*. The bacteriological test was the critical one, and in pertussis it was the only one on which reliance could be placed.

Referring to methods of immunization, Dr. Anderson said that the excellent brochure circulated by the Commonwealth

Department of Health and the leading article in THE MEDICAL JOURNAL OF AUSTRALIA of November 16, 1940, surveyed the accepted procedures. She could add little to them, except to reiterate the importance of the Phase I freshly isolated organism for the preparation of an adequate vaccine, and to plead for more rigid standards of diagnosis in pertussis and for a wider use of cultures for this purpose. A careless use of the phrase "This child has been immunized against whooping cough" might often give a false idea of security. As they had no evidence that a child, after receiving immunizing injections, had been in continued contact with another who was known to harbour *Hæmophilus pertussis*, they could have no certainty as to the success of their attempt to make him resistant to the disease.

DR. E. H. M. STEPHEN said that he was proud of being a personal friend of both speakers, especially after the excellent addresses they had just delivered. The discussion on immunization had been given in a manner that convinced one of its effectiveness. When the epidemic began in 1940, Dr. Stephen had read what he could of recent work on the subject and concluded that for satisfactory immunization a total of eight cubic centimetres of C strength Phase I vaccine was necessary and that smaller quantities were unsatisfactory. Dr. Stephen had thought that he must use eight cubic centimetres, and found it a dreadful thing to have to do, because the child thought that the doctor was always arriving and that he had no other method of expression than by needles. For his first half dozen patients Dr. Stephen did give the children eight cubic centimetres and felt very unpopular. His experience was that the quantity recommended was quite in excess of all requirements. In all his subsequent cases the doses he had used were practically on the scale Dr. Vickery had recommended in his paper, and he was satisfied this method had proved effective for this recent epidemic. With regard to the giving of the injection, Dr. Stephen preferred the intramuscular route. He had found that when the injection was given into the deltoid muscle the children suffered no reaction or discomfort. On one unfortunate day, on which he was immunizing children against pertussis and against diphtheria, Dr. Stephen had in mistake given the vaccine subcutaneously in one case. The child had a very bad night and the temperature rose to 104° F. Dr. Stephen always gave the vaccine into the deltoid muscle. Dr. Vickery had referred to the waves of virulence noticed in pertussis epidemics; Dr. Stephen said that one year the epidemic had reached its maximum in January and recurred not long afterwards. He thought that the explanation was that children who had had whooping cough and some contacts in Sydney had gone to the country for a change and had spread the disease there. Country children in their turn had then brought the disease back to Sydney. It was noticeable that the epidemic usually affected the country later than the city. The year to which Dr. Stephen referred had been prosperous, with a good season, and it had been possible for people from the country to come to Sydney and bring the disease with them. In the present epidemic money was more scarce and people were less inclined to move about, and consequently no second wave of epidemic had occurred. Dr. Stephen felt that Dr. Vickery's paper and its results should in some way, not only by its publication in THE MEDICAL JOURNAL OF AUSTRALIA, be brought before people, to make them realize that the dose of vaccine Dr. Vickery had mentioned was adequate, that such a dose did not need frequent injections; this would help to reduce the dread of the injections. In conclusion, Dr. Stephen congratulated the speakers again and said they had done a valuable service to the community in demonstrating the fact that those who had had considerable experience of this immunization were convinced of its value.

DR. C. C. P. WALKER thanked the speakers for their papers and referred to the trouble taken by Dr. Vickery in amassing the figures he had quoted. Dr. Walker said that there seemed to be no doubt of the value of immunization with vaccine. From Faber's summary of the results it was hard not to be convinced; he had decided that the 78% of children who were properly immunized did get full protection and that the other 22% got off with a very mild attack. There was a difference of opinion over the dosage, the method of administration and the age at which immunization should be attempted. Dr. Walker had treated over 100 children; all had received 80,000 million organisms. The vaccine was given in five doses, consisting respectively of 0.75, 1.25, 2.0, 2.0 and 2.0 cubic centimetres. Sauer had said that if children were to be protected, he thought this was the proper dosage, and that to reduce the dose was to take a great risk, and this required courage. It was difficult to determine when success had been achieved. Only five out of the 100 children treated by Dr. Walker had been definitely exposed to infection with pertussis, and they all had it in a very mild form. With regard to age, Dr.

Walker understood from Sauer that it was not much use attempting to immunize babies aged under nine months, because of their very poor antibody response. The immunization of very young babies, in Sauer's opinion, was not free from danger. Dorothy Gepp, in her article on the subject, had mentioned the inadvisability of giving the injections intramuscularly. Dr. Walker had always used the hypodermic route.

PROFESSOR H. K. WARD said that he had one thing to add to the discussion from the community point of view: What were they aiming at in the immunization of children against pertussis? How many of the susceptible children had they to immunize in order to make a dent in the mortality figures? The whole question turned on the effective inoculation rate. Diphtheria offered some analogy. The effective inoculation rate in that disease had been fixed by Ledingham as 80% of susceptible individuals. Only then, when that objective had been reached, was it possible to make a real dent in the mortality figures. Professor Ward thought that that statement was rather pessimistic and that 60% might be the figure. It was necessary to face the fact that any serious effort against pertussis meant that the State would have to undertake the immunization. If they asked the State to do it, where was it to be done? The infant welfare centres were obviously the place, but there would be opposition at once. They would be told to keep their hands off the welfare centres. They would also be up against the difficulty that Dr. Vickery had mentioned, that they had to prove that the immunity conferred was in the vicinity of 100%. People had to be educated up to the knowledge that no immunity was absolute, but that immunity was always relative. The figures from the Grand Rapids experiment were honest, and it was one of the few field experiments that would stand up to critical examination as having been carried out in a first-class way. It had proved that artificial immunity was real, but still only relative. It had also shown that natural immunity was also relative. It might be possible to persuade the State that immunity was relative, and that was the best that anybody could do, even Nature. Then it would be necessary to persuade the State about the question of reactions. That presented a great difficulty; the more vaccine that was given, the more chance there was that a reaction would occur. Dr. Vickery had wisely attempted to cut down the dose to half that recommended by Sauer. Sauer had done excellent work in putting pertussis immunization on the map, and people had followed his lead and given 80,000 million organisms as a standard dose of vaccine, and all the field experiments had been done on that basis. To carry out a really first-class field experiment was a big job; a huge amount of work was entailed. The Grand Rapids experiments were more valuable because they were carried out on a large number of children and with a large number of controls. To cut down the dosage of vaccine to one-half or one-quarter would call for another experiment of the same size. Professor Ward did not think that Sauer's experiments proved that the huge dose advocated by him was the optimum; Sauer was very dogmatic. He appeared to have set out to prove that immunity was absolute, and when a few of his treated subjects contracted pertussis he explained some of the infections by postulating that it took four months to establish immunity. Professor Ward said that it certainly did not take four months to establish immunity. One idea worth investigating would be the spacing of injections; but that could not be done at the beginning of an epidemic, when the chief object was to immunize everyone as quickly as possible. But now, in the absence of an epidemic, they could space the injections, preferably one month apart. If the State was persuaded to take on this task it would be taking on something more difficult than immunization against diphtheria. The main objections were the number of injections and the reactions that followed them. The American experiments had shown that, with a certain technique, it was possible to establish a worth-while immunity against pertussis. If that technique was modified to facilitate mass immunization, it would be necessary first to carry out a field experiment to prove the value of the modified technique. That would entail a great deal of work, but there was no short cut.

DR. LINDSAY DEY said that there was very little more to add to what had been said, except to thank Dr. Vickery and Dr. Anderson for their work. One other aspect of the matter had recently been put before the health authorities; that was the question of what precautions could be taken to prevent children suffering from the disease from going into public places, such as trams and theatres. "The powers that be" were very slow to move in the matter. Dr. Dey asked them what percentage of immunity they wanted to have guaranteed before they took up the question of immunizing children. It was impossible to guarantee 100%, and so they were loath to take up the matter. The main

thing was to educate the medical profession. Unfortunately, as Dr. Stephen had said, experiments with vaccine in the past had made it difficult to prove that immunization would be as effective as was now claimed. However, after the publication of Dr. Vickery's paper it should be possible to put the matter before the public.

DR. B. T. SHALLARD thanked the speakers for their papers. He said that in the city of Boston immunization against whooping cough was an accepted fact; there was no argument about it. It was "boosted" by the Commonwealth of Massachusetts health authorities by radio and all other means. It was difficult for the members of the medical profession to sell immunization to the public, because the public might think they had an ax to grind. It was better for some "middle man" to do this. The "B.M.A. Spokesman" had been able to do something in this way. If the members of the medical profession were backed up by the health authorities, they could publish the advantages of immunization. With regard to the days on which injections should be given, Dr. Shallard said that he understood that Sauer now recommended three injections of vaccine; the first was of one cubic centimetre and was given into one arm; three weeks later one cubic centimetre was given into each arm, and three weeks later again two cubic centimetres were given into each arm. Parke, Davis and Company put up the vaccine in ampoules of seven cubic centimetres capacity. Dr. Shallard had just treated some children in this way; but he was unable to estimate how much immunity had been conferred. It was difficult to induce parents to agree to the procedure. Dr. Shallard thought that all the members of the profession could treat some children, and all could talk about the work; more immunization should be got going in Australia.

DR. E. S. STUCKEY expressed his appreciation of the papers. He said that there was one pressing question, namely, what were the members of the profession to advise patients? The Government was disinclined to do anything in regard to pertussis immunization. It was difficult when between epidemics parents asked whether their children should be immunized against pertussis. Dr. Stuckey still did not think that there was enough evidence on one or two points. First of all, had there been any proof as to how long natural immunity lasted after an attack of the disease? Dr. Vickery had said that immunization immunity lasted approximately as long as natural immunity. Secondly, in the administration of the vaccine, should it ever be given at intervals of less than one week? Dr. Vickery had given the impression that he gave the injections at intervals of two days. Doctors tended to extend the time interval to one month. Again, should the injections be given subcutaneously or intramuscularly? Did the pathologists think that better immunity could be achieved from subcutaneous injections than from intramuscular ones? Dr. Stuckey thought that in the present state of knowledge and at the present stage of the Government's apathy he should advise parents to wait until an epidemic occurred and then to let him treat their children.

Dr. Vickery, in reply, thanked those who had taken an interest in the discussion. He said that there were a number of questions, of the answer to which he was not absolutely certain. He thought that Dr. Stuckey's questions might be best answered by Dr. Anderson. Dr. Stuckey had asked how long natural immunity lasted after an attack of pertussis. Dr. Vickery said that patients did contract the disease twice, but that was on rare occasions. It was not as unusual as they imagined, perhaps, and it occurred in elderly people also. An attack did give a good guarantee that the subject would not contract the disease again. With regard to the dosage of 70,000 million or 80,000 million organisms, Dr. Vickery said that in 1933 the Grand Rapids experiment had been in progress for fully five years and the same children had been under observation; they had been exposed to infection with whooping cough and they were not contracting whooping cough. But the point that Dr. Vickery wished to make was that if these children did contract the disease they were now of an age when they would not lose their lives. It was possible that a community of adult "whoopers" was being bred, but only time could prove that. With regard to Dr. Stephen's remarks concerning the use of the intramuscular route for the injections, Dr. Vickery said that he was afraid that he himself had used it in a number of cases in the past. But from all that he had read he thought that if the vaccine was given subcutaneously it had more chance of producing more active and more lasting immunity. Dr. Vickery was interested in Dr. Stephen's explanation of the "false epidemic" of 1934; Dr. Vickery thought it quite feasible. He had often noticed that an epidemic died out in the school holidays and broke out again later. Dr. Vickery then referred to the hundred children that Dr. Walker had treated. If children went to be treated during an epidemic period, they

should be immunized with increasing doses every third day, according to the reaction, commencing with 0.5 cubic centimetre (5,000 million organisms), in the case of babies under three months of age 0.25 cubic centimetre (2,500 million organisms). With regard to reports concerning the treatment of children aged under six months, several fatalities were stated to have occurred in the United States of America. Dr. Vickery had read the literature, and the reports were not to him entirely convincing. One or two deaths had been reported. Dr. Vickery himself had given the vaccine to very young babies to protect them and had had no reaction that had caused him any concern whatever.

Dr. Phyllis Anderson, in reply to Dr. Stuckey, said that she could not be very comforting. Absolute proof of immunity, as she had said before, existed only in an exposure of the immunized child to infection, and she did not know an absolute test of immunity. A second attack of whooping cough was not unknown, and there were also many instances of a recurrence of symptoms without the recovery of organisms. Whether this was due to a "fade-out" of immunity, Dr. Anderson did not know. It was a well-proven fact that material given by the subcutaneous route was more slowly absorbed than that given intramuscularly. This was certainly true of antiserum and vaccines, and the aim in producing immunity was that the stimulus should be slowly absorbed. The subcutaneous route was more generally used. Dr. Anderson then referred to the discussion that had taken place on the size of the doses to be administered. She said that, as Professor Ward had pointed out, the task of assessing the respective merits of small doses and large doses was a colossal piece of work, and the only control experiment of which she knew was the Grand Rapids experiment, in which were 126 partly immunized children, among whom the attack rate approximated that in the fully protected. This seemed to show that perhaps smaller doses might be effective. Dr. Anderson had no knowledge of the ages of these children. She thanked Professor Ward for expressing so clearly the fact that the effective inoculation rate had to be recognized and adequate if immunization against pertussis was to be attempted. It had to be done on a sufficiently large scale.

Dr. WILFRED VICKERS, from the chair, said that those present were extremely grateful to the reader of the paper and to those who had joined in the discussion for throwing much light on the subject of pertussis immunization; it was extremely important from the public health point of view. There was evidence that practitioners in other States had had patients go to them and ask about pertussis immunization as a result of a broadcast talk by the "B.M.A. Spokesman"; the patients had mentioned the talk. Dr. Vickers said that it was gratifying that positive results were following this broadcast talk. Another matter to which he wished to refer was the necessity for all medical practitioners to take a greater interest in informing public opinion on the question. The public health authorities for various reasons seemed very slow to move, and Dr. Vickers thought when the case was put as Dr. Vickery and the other speakers had put it, the evidence was so satisfactory that immunization must be regarded as being of value in spite of some differences of opinion. It would be justifiable now for any members of the medical profession to tell anybody who inquired that there was good evidence that any child had a 75% chance of contracting whooping cough, and if the child was aged under two years it had a good chance of dying from the disease or of suffering considerable morbidity. There was evidence from the Grand Rapids experiment that this risk could be minimized. It was possible to give people that information; and Dr. Vickers hoped that the members of the profession would be more public-spirited and tell the public about immunization, bringing pressure to bear to have the matter seriously discussed. Dr. Vickers then referred to certain areas in which "anti" people were active; an example had occurred at one centre, where a lay practitioner had spoken against diphtheria immunization, giving frequent broadcast talks on the subject. This had been stopped; and since then there had been a rush to have children immunized against diphtheria. That was the point of view that Dr. Vickers wished to put before the members, and he wondered how Dr. Vickery's excellent paper and the discussion could be utilized so as to have a far-reaching effect. Those present owed a debt of gratitude to the speakers.

A MEETING of the Victorian Branch of the British Medical Association was held on July 2, 1941, at the Medical Society Hall, East Melbourne. Dr. H. BOYD GRAHAM, D.S.O., M.C., the Acting President, in the chair. The meeting took the form of a symposium on "Common Affections of the Ear, Nose and Throat".

Inflammatory Conditions of the Mouth and Pharynx.

DR. RAYMOND HENNESSY discussed acute inflammatory conditions of the mouth and pharynx. He said that he had often thought it a nice point for doctor and patient to decide which was the more distressing, an acute inflammatory condition of the first three inches or of the last three inches of the alimentary canal. Inflammation at either site was common and created difficult clinical problems. Most of the errors in diagnosis were due to inability on the part of the doctor to see the lesion. Ordinary methods of examination were quite inadequate for deep inspection of the pharynx. A good focusing torch or a headlight was indispensable, because a patient with an abscess in the mouth or throat was unable to open his mouth fully, and the parts were swollen and distorted and obscured by the secretions. A common example was quinsy; none of those present was likely to have escaped the experience of being deceived by quinsy, either by mistaking it for something else or by assuming pus to be present when it was not. In Dr. Hennessy's opinion one of the commonest errors was the confusion of acute inflammation of the tonsil with peritonsillar abscess. The medical practitioner, when he saw bulging of the palate, was likely to conclude that suppuration had occurred; but the bulging might be due merely to great enlargement of the upper pole of the tonsil forcing the soft palate towards the buccal cavity. Dr. Hennessy reminded his audience that, like other glands, the tonsil increased in size enormously when inflamed, the length as well as the circumference being affected. He went on to say that there were some useful clinical rules that helped in the accurate diagnosis of these lesions. It was a curious fact that quinsy, as strictly defined, was never seen in patients aged under ten years, though at times youthful doctors reported in medical journals the observation of quinsy in patients of four or five years of age; such a statement should be accepted with the utmost reserve. It was probable that the doctor would be describing an intra-follicular abscess of the upper pole of the tonsil—intra-tonsillar and not peritonsillar. It was not correct to regard the distinction as just "Tweedledum and Tweedledee", because the treatment in the two cases was quite different. The intratonsillar abscess should be allowed to break naturally and should not be incised; but the peritonsillar abscess should always be opened.

Dr. Hennessy then said that the chronology of disease was illustrated also in acute retropharyngeal abscess, another condition simulating quinsy. That condition occurred in infancy and generally in the second year of life, and was never seen after the age of three years. It was not cellulitis, but suppurative adenitis of one or occasionally of both of the lymph glands located opposite the body of the second cervical vertebra. When the condition was unilateral the palate was pushed forward, and the first impression gained on examination was of the swelling of the palate itself; headlight illumination was essential for a decision. If a patient aged under three years was seen with a bulging palate, the probable diagnosis was retropharyngeal abscess; if the patient was aged between three and ten years, it was acute tonsillitis; and if the patient was more than ten years old, it might be peritonsillar abscess. Dr. Hennessy went on to say that a helpful diagnostic point in quinsy was that the patient had extreme difficulty in opening the mouth and much more difficulty than in the other two conditions. Another sign was that only a quinsy would be exquisitely tender if a finger or probe covered with cotton wool was pressed on the swelling; there was nothing so tender in the body as a recently accumulated collection of pus under pressure. A third point in the diagnosis of quinsy was the observation of displacement of the uvula.

Dr. Hennessy then spoke of two other conditions which closely simulated quinsy and were often mistaken for it. They were abscess of the tongue and abscess of the floor of the mouth. He said that a true lingual abscess was usually in the posterior third of the tongue and that a useful diagnostic point was that the patient, although able to open the mouth, could not protrude the tongue beyond the incisor teeth—the opposite to what occurred in quinsy. The abscess in the floor of the mouth was usually ascribable to infection around a stone in the submaxillary salivary gland. The orifice of Wharton's duct in such a case would be everted, red and pouting, and a small stone might be seen extruding from it.

Dr. Hennessy added that an abscess around a molar tooth, usually a wisdom tooth, might also simulate quinsy; trismus would be a conspicuous feature and the movements of the tongue would be impaired in each case to a less degree than in the other conditions under consideration. He said he had also known a mistaken diagnosis of quinsy made when the condition was an abscess following mandibular nerve block injection for the extraction of teeth; the dental

surgeon injected the local anæsthetic agent into the loose areolar tissue between the pterygo-mandibular ligament and the ramus of the jaw. That condition was successfully treated by aspiration, blood-stained, evil-smelling pus being obtained. It was generally a low-grade infection, as aspiration appeared to be adequate for its relief. In those cases Dr. Hennessy had observed that earache was a prominent feature.

Affections of the Ear.

DR. JOHN SHAW, in discussing common affections of the ear, dealt first with external otitis, which he divided into two large classes, the moist and the dry. In dealing with the dry otitis he stressed the importance of recognizing that quite often there was an underlying seborrhoea of the scalp, which, if not effectively dealt with, would lead inevitably to a relapse of the ear condition. Superimposed on the seborrhoeic basis was a staphylococcal infection, and for that reason he believed that a solution of gentian violet (1%) and neutral acriflavine (1%) in alcohol (20%) was the best method of treatment. Ointments were unsatisfactory in a cul-de-sac such as the external auditory canal.

The next subject discussed by Dr. Shaw was furuncle of the external ear. He was opposed to incision unless actual pointing was present; but if the lesion was to be incised light general anæsthesia should be employed. He went on to say that recurrence was often due to surface reinfection by staphylococci, and a great deal could be achieved by adequate disinfection. If recurrence still persisted, a careful survey of the general health was essential; glycosuria, anaemia and dietetic deficiencies and excesses had to be excluded. He considered that "Uleron" was a useful, though somewhat too potent, drug upon which to rely.

Dr. Shaw then emphasized the necessity of distinguishing between simple myringitis and a true middle ear condition. The former was characterized by suddenness of the onset with pain, which was excruciating but of short duration. Though the hearing remained good, the appearance of the drum membrane was characteristic, in that the superficial epithelium was raised in large purplish blebs; but the anatomical landmarks could still be discerned. The treatment should be minimal, consisting at the most of the use of sedative hygroscopic drops. On the other hand, in the consideration of an acute middle ear condition the importance of affections of the nose and throat was stressed. The middle ear was but another nasal accessory sinus and was subject, therefore, to all the infections of those tracts. In treatment the incision in the drum membrane should be as large as possible, and great quantities of citrated fluids should be administered with the object of obtaining a profuse outward flow. Dr. Shaw said that if that object was attained, drops were not needed in the early stages, and he doubted whether they ever did more than establish mild antiseptics of the external auditory canal. He remarked that such an ear should be dry in ten to fourteen days and that if with efficient treatment it was still moist with discharge after twenty-eight days, simple mastoidectomy should be performed to ensure that normal hearing would be restored and to avoid chronic *otitis media*, which might possibly have serious complications.

Acute Nasal Conditions.

DR. T. G. WYNNE discussed the diagnosis and appropriate treatment of some of the acute nasal conditions which were likely to be met with in general practice. He began with injuries to the nose, which he said were usually the result of direct violence and should receive early treatment to prevent vicious union of the septum or nasal bones, which might be broken with displacement of the fragments. If there was much swelling, reduction of the fractures should be carried out under general anæsthesia, though the local use of cocaine and adrenaline was adequate at times. The fragments could be maintained in position if the nose was packed with "Vaseline" gauze, which should be removed within twenty-four hours.

Dr. Wynne went on to say that hæmatoma of the septum due to violence might occur without external deformity, and if it was causing inconvenience it should be aspirated or incised, particularly as it was subject to suppuration. It was advisable to tuck a strip of gauze into the lips of the incision after the clot was expressed. If a hæmatoma became infected an abscess of the septum would develop, causing throbbing, heat and tenderness in addition to nasal obstruction. As there was a grave risk of necrosis of cartilage, which might produce deformity by depression of the bridge of the nose, prompt incision was indicated.

In discussing furuncle of the nose Dr. Wynne said that the usual site was high up in the attic, and as in that position the skin was tightly bound down to the cartilage, a furuncle was very painful. If the patient was examined

at an early stage the centre of the furuncle should be touched with pure carbolic acid on a probe or with a diathermy point. In no circumstances should a furuncle be incised or squeezed, on account of the risk of precipitation of cavernous sinus thrombosis. Dr. Wynne then spoke of epistaxis. He said that the common site of the bleeding was Kiesselbach's or Little's area, situated 0.5 centimetre inside and the same distance above the floor of the vestibule; there the fine arteries anastomosed and the mucous membrane was very thin. The bleeding might come from one definite spot or be the result of oozing from the whole region. If a firm pledget of cotton wool was placed over the bleeding area and pressure was maintained against the outer side of the nose firmly for ten minutes the bleeding could usually be arrested. Especially in the case of young people it was advisable at a later date to touch the dilated vessel in one or two spots with a cauterizing agent, after blanching the area with a solution of cocaine and adrenaline. Hemorrhages in other situations were nearly always due to hypertension or toxæmic conditions or to local conditions such as a newgrowth. The nose should be cleared of clots and packed with gauze soaked in cocaine and adrenaline solution. If the bleeding point could be found it should be cauterized, but if not, the nose should be packed with gauze containing one part of Friars' balsam in two parts of "Vaseline".

With reference to foreign bodies, Dr. Wynne drew attention to the importance of remembering them when children had nasal obstruction or purulent nasal discharge, especially if the trouble was unilateral; in the course of time lime salts might be deposited on a foreign body, which might become the centre of a rhinolith. Any condition of partial or complete nasal obstruction might lead to hypertrophy of portions of the nasal mucosa and to an excessive secretion of mucus giving rise to nasal catarrh, which was a common complaint. The commonest causes were hypertrophy and infection of the adenoid tissue and chronic sinusitis; but Dr. Wynne said that time did not permit of full consideration of the special methods of investigation and treatment of those causes. Other causes were deflection of the septum or the presence of spurs along the crest of the vomer and increased swelling of the erectile tissue of the inferior turbinates, which was usually intermittent and might vary from side to side within a few minutes during an examination. Occasionally the anterior end of the middle turbinate might have an air cell in it large enough to cause obstruction. If the mucosa on inspection, instead of being reddish, was found to be of a pale bluish colour, sodden looking and swollen, the condition was almost certainly dependent on hypersensitivity to some irritant; the irritant should be identified if possible and desensitization attempted, as local treatment was usually unsatisfactory.

Another cause of nasal obstruction and catarrh mentioned by Dr. Wynne was the presence of polypi, usually arising from around the middle meatus and the margin of the middle turbinate; but he said that at times the ethmoidal air cells and antrum might be packed with them. If they were few in number they might be removed with the snare, with fair prospects of cure; but if they were numerous they were prone to recur until the underlying infection in the sinus received radical treatment. Antro-choanal polypus, which not infrequently occurred in childhood, was a large simple polypus presenting in the posterior choana or naso-pharynx; it was sometimes mistaken for naso-pharyngeal fibroma. If the nasal mucosa was shrunk with cocaine and adrenaline solution, it was usually possible to see either the stalk or the glistening polypus far back in the nose; but it was better to use a post-nasal mirror or to make a digital examination of the naso-pharynx. The polypus could be removed either by a snare through the nose, assisted by the finger in the post-nasal space or by avulsion after the pedicle had been grasped with nasal forceps. After its removal there was little tendency for it to recur.

Affections of the Larynx.

DR. ERIC GUTTERIDGE discussed some common affections of the larynx. He demonstrated the anatomical features of the various conditions by means of lantern slides. Dr. Gutteridge referred first of all to *laryngismus stridulus*, and he spoke particularly of the abnormal flaccidity of the upper laryngeal aperture as the underlying basis, valvular closure on inspiration giving rise to the symptoms.

Dr. Gutteridge described Heaf's four groups of tuberculosis of the larynx and discussed the treatment appropriate in each case. In epiglottico-arytenoidean tuberculosis, infiltration, oedema and ulceration occurred, affecting all the structures of the upper aperture. The prognosis was bad and the duration of life was usually inversely proportional to the extent of the ulceration. In corditic and interarytenoid tuberculosis, as long as the arytenoids remained unaffected the prognosis was fairly good. In single cord affection or

affection of two small areas opposite each other, and in granular or smooth tuberculomata, a relatively good prognosis could be given.

Dr. Gutteridge then discussed intrinsic and extrinsic carcinomata of the larynx, and showed lantern slides of post-cricoid and mid-oesophageal carcinomata. He said that laryngo-fissure with subperichondrial removal of the cord and tumour in the treatment of carcinoma of the larynx was losing favour in comparison with Harmer's window resection and radium implantation. Dr. Gutteridge concluded by urging the importance of early diagnosis and the use of the laryngeal mirror in the routine examinations, aided by local anaesthesia with "Decicain" solution.

Correspondence.

WHO GROWS THE CABBAGES?

Sir: The country members of the British Medical Association (I am one) have long reserved to themselves a special prerogative in the matter of grumbling—criticizing especially schemes for the regulating of our practices, put forward, without our collusion as we think, by the State and Federal councils.

We are making the mistake of attributing to the executive members of the councils the faulty results which spring from defects in the constitution of the British Medical Association itself.

The Association has become very large and powerful, because it claims to speak in the name of all the doctors, and it is no longer democratic enough for all its claims and needs; the claim is often false, when the executive would welcome support.

We are blinded to this by a happy feeling of comradeship and goodwill between all of the members—council, executive and subscriber alike.

The Association is not democratic because:

1. There is no official "opposition" to air criticism and complaints during council sessions. Instead there is only the opportunity of grumbling after the decisions have been formed, and costly devices are adopted to reverse them—not the least costly devised indirectly in the loss of Mr. Abraham's life.

2. Present-day conditions limit nominees to council to urban practitioners in the capital cities. This is due to the fact that councils meet only in the capital cities, and as the practices have to be worked, a deterrent load in time and transport is carried by any doctor practising outside these cities.

So in fact (though not in theory) nomination for the council is no longer open to any member of the British Medical Association, but to a limited few.

The same difficulty applies to attendances at meetings; and a lack of contact has resulted, without provision for letting the executive know it till the boiler reaches explosion point: by that time tempers are up and sensitivity to criticism is produced. This is autocracy, however unconscious.

Great changes are about to take place, not in our livelihoods only, but in our whole life's work. Can an unrepresentative executive carry us through this successfully and with content?

The British Medical Association failed in England at this juncture; it thought chiefly in terms of money—capitation fee *versus* popularity with the general public—and hardly at all in terms of the doctor's soul. I would designate as a doctor's soul: "The opportunity to make use of the skill trained in him. Leisure just sufficient (if no more) to read and watch to maintain or better his professional standards, when qualified." To some this would mean a share in the use of hospitals and an adjustment of working hours per day; to others perhaps other things, but some free time.

With unlimited hours the standard of living goes down, not in money perhaps but intellectually, and in the joy of living; instead comes a sense of being threatened if you stop.

When the extent of the national insurance practitioners' liabilities was appreciated in England, we rightly blamed the British Medical Association, but wrongly blamed the negotiators instead of the constitution of our machine.

Numbers left the British Medical Association in their wrath, yet the executive told us we were apathetic, and the disaster was the result of our "apathy". A rival "Practitioners' Union" prevented further disintegration by forming an official "opposition".

Now history is repeating itself; the executive feels something is wrong. A leading article in THE MEDICAL JOURNAL

OF AUSTRALIA has already told us we are "cabbages" unless we welcome? criticize? help initiate? or what? some unspecified scheme for national medicine; all one can see clearly is that the Federal Council is already at work on something together with the Government and are anxious for support; perhaps to know our views. We cannot give them; even if we all had facility of written expression, a mere flood of letters would be useless without knowledge of what is relevant.

And we feel the councils may not enable us to speak till too late to make our viewpoint felt during the drafting of the scheme. Let us collaborate, not assent afterwards.

Can we not create a better parliament out of the Association? At present we have a one-party government, no opposition, no *Hansard* and practically no account of discussions in council, no referendum.

As an outline for forming some constructive scheme the following suggestions are offered:

1. The allocation of geographical areas to each State council member, together with a part-time personal clerk; it would then be this member's duty to see that a confidential circular letter was sent to each individual doctor in his area, reporting discussions on which conclusions had been formed (except those few taken *in camera*). This member's job would be distinct from that of the Branch secretary, who is not present in council. Occasional reports in the journal will be missed, in the absence of leisure to digest the whole paper, and so they are. Important matter is often printed for our information on the back of the agenda sheet of the British Medical Association monthly meetings; these words are instructional, and quite apart from the collusion type of information required to inspire confidence. Unless we get early informed knowledge, which breeds confidence in return, the executive will continue to have "cabbages" for members.

2. A frequent use of a referendum on all important questions of policy, the answer being returned in writing. Such matters are now decided at meetings by a show of hands. These meetings represent chiefly the practitioners living near by and able to come; are therefore not very representative, and the method of voting does not give time for reflection after hearing the arguments discussed.

Do you favour capitation fee or fixed salary?

Do you consider "free choice of State doctor" essential, or should patients be allocated to their nearest practitioners? What do you fear most in a national medical service scheme?

These would be suitable subjects for referendum inquiry; and any other points of general policy.

3. A lower and upper age limit for members of council. A man too young has no, or little, experience of conditions and liabilities in general practice and its risks. A man too old has but few working years in front of him; his personal desire is rather for peace and comfortable relations with authority during the few remaining years. Sacrifices for appeasement might make an undue appeal to such a man, and one suspects they sometimes do, and make him unduly fearful for his brother's livelihood. But his brother may have twenty years to go, enduring the appeasements. I would make an exception for members of an ethical committee.

Time is very short; broadcasts and newspaper articles show that plans for a national medical service must be already under discussion, and we must believe the Federal Council is taking some hand now.

If every member who may read this letter would tear it out of the journal, then mark approval of points with a marginal red line, and disapproval by deleting the paragraph with ink, and post the resultant effort to his Branch secretary without delay, it ought to help. Even if the letter arrived scored throughout with disapproval by you, much could be deduced from that as to your wishes.

I do not suggest they will, but if our British Medical Association executive officers should turn out also to be "cabbages" when faced with a demand for constitutional reform, might we not ask that they should set the pace first in making concessions for democracy? The democracy of the profession.

And on our part, may we never forget amidst our grouches that the council gives unstintingly its labour and its time—sacrificing its leisure for the common good, with all such vision as it has—and it needs more—ours! The general practitioners in the country.

It is up to us; please decorate this letter and post it, as you see fit.

Yours, etc.,

O. N. WALKER.

Mount Barker,
Western Australia,
August 6, 1941.

CHANGES IN THE LUNGS IN VARIOUS INDUSTRIES.

Sir: In the homage to Lister entitled as above in your journal of July 26, 1941, Dr. J. G. Edwards is weak on his facts.

I decline to believe that he has reached that age when we prefer our opinions to other men's work, nor do I deny his right to his own opinions in such things as are lacking reasonable scientific proof, but I consider that he ignores the literature of the past ten years and that his account is generally inaccurate.

I will only be able in a letter to point out a few of these errors.

"The risk of contracting silicosis is in direct proportion to the pure silica content of the dust." This is not so; some dusts with a large percentage of free silica, for example, shale, do not produce silicosis. A great deal of work has been done in the past ten years on the protective action of various minerals against silicosis. (I.L.O. Silicosis Conference, 1938, page 209.)

"After sixteen years of this practice no new case of silicosis had occurred in the Broken Hill mines." Is it in Dr. Edwards's knowledge that the men who have spent sixteen years in the mines have all been radiographically examined at the end of this period? There is no published record of it.

"Further, in many dusty mines there is a practice of blowing sand into the workings in order to carry coal dust to the floor and prevent the risk of explosion of a mixture of fine coal dust and air." This is a reprehensible statement; it has never been the practice in this State to stone dust the coal mines with anything but shale, limestone or flue dust.

"Coal contains from 3% to 5% of silica." The coal of the pit in which occur most cases of coal miner's lung in this State contains but one-half per centum of free silica.

"The foregoing points certainly explain all the phenomena associated with this condition of silicosis." This is a happy thought but . . .

"Lastly, let me refer to the question of compensation of individuals exposed to these serious industrial hazards. In New South Wales there is a special Workmen's Compensation (Silicosis) Committee, which considers the application for compensation by these injured workers." This is less than half the story. There is a special compensation act for Broken Hill which deals with the miners there, but the main tribunal for dust diseases in New South Wales is the Workers' Compensation Commission, which deals with the majority of cases, and this tribunal is distinct from the Silicosis Committee.

In one thing I am with Dr. Edwards, and that is the inability of radiologists to diagnose emphysema, and particularly the form which is characteristic of coal miner's lung. He says (and I never hoped to see the day): "Many radiologists, with a certain abandon, regularly diagnose it; but I am afraid that it is only guess work."

When, I wonder, will radiologists drop that abandon and guess work which leads them to suppose that they may separate dust lesions from tuberculosis, for using the same lymphatic vehicle, dust and tubercle cause similar lesions?

In conclusion we have in the report of the Royal Commission on the Safety and Health of Workers in Coal Mines (Sydney, 1939) a masterly presentation by Mr. Justice Davidson on dust and dust diseases.

No radiologist writing on industrial lungs nor any industrial hygienist can afford to neglect it.

Yours, etc.,

CHARLES BADHAM.

Department of Public Health,
Sydney,
August 14, 1941.

A "NEW" TREATMENT FOR ARTHRITIS.

Sir: I have received within the past few weeks a large number of inquiries regarding a "new" treatment for arthritis, details of which had evidently appeared in the Sydney Press.

Not being an ardent newspaper reader, I was unaware of this, and had to procure the particular issues to find out what was actually the promised cure. It transpires to be our old friend the vaccine—resurrected and apparently endowed with enhanced potency.

Now, in the course of twenty years' interest in what recently has been labelled "rheumatology", I have been familiar with the work of Warren Crowe, and I have seen

in 1926, at Harrogate, some of his cases which were treated by his vaccine. Further, I have a great admiration for the years of experience, the painstaking research and the unabated devotion to a principle displayed by a man of his undoubted ability. For example, Crowe has been working on vaccines and arthritis for over thirty years, and his stock vaccine at one time took two years to make and was said to contain over one hundred and fifty strains of streptococcus! Other staunch devotees of the vaccine treatment of arthritis were the late Dr. Munro, of Bath, and Professor Crofton, of Dublin.

I myself have used vaccines—vaccines of all kinds—English, American, Irish, French, Australian, German and Japanese—stock and autogenous. Perhaps I do not know how to use them, perhaps they were not the right strains, perhaps the cases were unsuitable; but I have not seen any results that could not have been bettered by other means.

The point I wish to emphasize is this. I believe that arthritis is a far too complex disease to be treated successfully by any single therapeutic measure, and while this "new" vaccine may be different from all its predecessors, I think that it is rather unwise to awaken false hopes in people whose arthritis may be much too advanced for any vaccine to "cure".

My own view of the etiology of arthritis—osteo- or rheumatoid—is that many factors are usually at work.

Physical trauma—often of long duration—vitamin and calcium deficiency due to unbalanced diet, psychological disharmony and emotional strain, toxic absorption—usually overstressed—endocrine dysfunction and faulty tissue metabolism and skin excretion may be mentioned.

The term "rheumatic diseases" comprises at least fourteen clinical entities, and, as I believe, all related and, very often, stages in the body's reaction to some or all of the above causal factors.

I find it difficult to see how one single item of treatment can rectify adequately a profound and long-standing metabolic disturbance.

In arthritis one should treat the body as a whole—and usually the mind—and visualize both working in healthy coordination, if one is to achieve what I consider a successful result. To treat a symptom alone, such as a neuritis or fibrositis or monarticular arthritis, is just as intelligent a procedure as pouring a can of oil into a worn-out car engine.

One aspect of the problem which I noticed as featured in the lay Press is that of the desirability of the Government establishing arthritic clinics in the large cities of Australia. This is a matter of very great urgency and importance and is one which I have advocated repeatedly, especially in the issue of THE MEDICAL JOURNAL OF AUSTRALIA dated July 3, 1937. I would wish to emphasize now what I said then.

War or no war, the health of a nation is a government's primary concern, and the ravages of arthritis may be imagined from the reports that in Sweden 35,000 persons are totally disabled, in Germany 75% of industrial workers over forty years of age suffered from rheumatic diseases a few years ago, and that in England the same diseases cost the country over 20,000,000 pounds sterling yearly.

Yours, etc.,

E. HASLETT FRAZER.

231, Macquarie Street,
Sydney,
August 15, 1941.

MEDICAL SOCIOLOGY.

Sir: It was a pleasure to read your journal of August 9, with Dr. Dale's and Dr. Mailer's papers on medical sociology, the discussion on them, and your editorial. It is cheering to see that our profession is awakening to the economic implications of its work among patients, to the fact that unemployment and the fear of unemployment (insecurity and insufficiency!) are important causes of ill health, and that there should be an inquiry into the whole question, especially into the financial system.

We are not alone in our perception of the economic evils of the day. Much of the literature of the day, for example, "The Grapes of Wrath", "Love on the Dole", "Nobody Starves" *et cetera*, presents what may be called the case for commentary. What is the cause of these evils? And what can be done about them? We need to do more than "assess and advise"—we should bring our diagnostic powers to bear on our economic problems—indebtedness of the primary producer, unemployment, malnutrition of the oncoming generation, and strikes, to say nothing of war! It is not enough to organize the medical profession—that will but reduce liberty for both doctor and patient, without touching the real problems facing men, women and children.

A glance back at history shows that there has been a constant struggle between the desire for liberty and the desire for security. The serf, secure through his tie to the soil, craved liberty so much that he bought freedom with all its insecurities (perhaps he knew not what he did!); we, formerly so free personally, are now sacrificing our freedom for security (perhaps we know not what we do!), consenting to, even seeking, regimentation and dictatorship. The truth is that under our existing system of exchange (finance) it is impossible to achieve both freedom and security. Once this is realized we shall certainly insist on a "radical overhaul". "Safety first"—security without freedom—will never satisfy the Anglo-Saxon, grounded as his tradition is in personal freedom; while he, like other men, does not live by bread alone.

The medical profession should join in with the Mildura movement for national and social reconstruction in demanding that the principle of our religion—that we are a family and should live as a family—be applied to our financial and economic system, and require from the Government a royal commission to inquire into the theory of money.

Yours, etc.,

MARY C. DE GARIS.

Geelong,
Victoria,
August 16, 1941.

MEDICAL EXAMINATION OF ARMY RECRUITS.

SIR: I do not know whether you publish letters from non-medical men, but I think the matters I propose to raise are of such vital importance to the medical profession that doctors engaged in examining recruits for military training should give them serious consideration.

As a premise, I maintain that conditions under which these medical examinations—or, at least, the one of which I had personal experience—are conducted, would revolt a medical man of pre-Lister days.

Firstly, in a small room, about 12 feet by 12 feet, recruits were required, in the presence of five or six other recruits, to produce a specimen of urine. For this purpose a cream jar, dirty in appearance, was provided. There were five cream jars, about 200 recruits. Each jar, therefore, was used on the average by 40 recruits. After the urine tests were made by a military non-commissioned officer, excess urine was poured into a bucket and the jar, not even rinsed, handed to another recruit. It is almost impossible to urinate in such a jar without some contact being made. Even if this were possible, there is still grave danger that in holding the jar gonorrhoeal matter—or worse—will be communicated to the hands. Medical men do not need to be told that such matter on the hands can be communicated to the eyes with astonishing rapidity. How any conscientious doctor in charge of an examination could tolerate such primitive methods, which are contrary to all fundamental principles of hygiene, is beyond me. But they do!

The room in which examinations were held appeared to be about 30 feet by 15 feet. It was partitioned at two-thirds of its length by a curtain. There was a large gap between the curtain and the wall, which gave men waiting in the smaller section a full view of recruits being examined. It was a cold day—in June. Yet a doctor told each man to take off all his clothes ready for examination. I personally waited fifteen minutes in the nude, unpleasantly aware of the cold. The floor was grimy, and by the feel of it in bare feet, an excellent place to contract tinea. Some of the men stood, others had the temerity to sit on a long, much-used bench in the nude. I hope they have not regretted it since! The examination was carried out efficiently, but with complete disregard for privacy, to which most men feel they are entitled. Any general practitioner who showed the same lack of consideration would be bankrupt in a month.

Men in the examining room with me touched their toes, squatted, and were examined for piles in the presence of each other and before an audience of self-conscious men in the next room.

Those are my main complaints. British Medical Association members might say: "But these things don't concern us. We deplore them, but it is a matter for the military." But is it? What doctor would tolerate such unhygienic conditions in a private hospital, where, strictly speaking, he had no control over the preparations made for an operation or clinical examination?

Nor do I complain merely that the conditions would be a disgrace, from the point of view of hygiene, to an uncivilized community.

Medical examination, to many men, induces a state of nervousness and excitement which might cause unfavour-

able signs—rapid pulse, abnormal blood pressure *et cetera*. Yet no attempt is made to put men at their ease. No man—or very few—likes to be examined for piles in public. Even if this and other phases of the examination—such as urinating publicly into filthy jars—have no effect on clinical findings, each man is entitled in a military examination to the same consideration of his feelings that he expects and receives from a private practitioner. Heaven help the "G.P." who was not solicitous of his patients' right to privacy.

These matters are so easily rectified that I think the British Medical Association should insist that adequate hygienic examination cubicles, where men could be examined privately, should be provided. Otherwise, I fear the prestige of doctors will suffer worse damage than I think these primitive practices have already caused.

Yours, etc.,

"RECRUIT."

August 16, 1941.

THE NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL.

SIR: I note in your leading article that the National Health and Research Council is of opinion that in general alien medical practitioners should not be allowed to practise in remote places for apparently two reasons: (1) That the Continental system of training renders many of them unsuitable. (2) That after the war there may be an influx of such doctors.

As regards their suitability, some are suitable, but no systematic examination of their capacity has been made. In the Victorian Bush Nursing Association some previously registered have made good.

As regards the future, that is in the hands of the Immigration Department. Apparently aliens can enter and do prove useful if they are not medical practitioners.

In the meantime what is to happen in districts which have no medical or nursing aid, especially in the case of women and children? The Victorian Bush Nursing Association has a number of such districts in want of medical aid. They would prefer Australians, but if they cannot get them they ask for aliens.

Two or three months' post-graduate work would enable some of them to fulfil Australian conditions. In one case I personally arranged for some post-graduate work.

Finally, it is useless to tell the countryman, working hard and rearing a family, that he must wait for governmental action, which from its very nature is slow and cumbrous.

It is not a matter of money, but definitely of shortage of doctors, which will probably increase as the war continues.

But the recommendation contains an important escape clause. Discretionary power is to be given to medical boards to register those who have undergone training equivalent to that obtained in Australian universities (when and how). If this provision is put into practical service and wisely used, with or without post-graduate work, the position will be made much easier. But at present in many districts the position can only be described as deplorable and almost barbaric.

Yours, etc.,

JAMES W. BARRITT.

103-105, Collins Street,
Melbourne, C.I.,
August 18, 1941.

Obituary.

ALBERT WILLIAM SHUGG.

We are indebted to Dr. W. E. L. H. Crowther for the following appreciation of the career of the late Dr. Albert William Shugg.

The news of the death at only forty-eight of Dr. A. W. Shugg did not come unexpectedly to his friends and patients. For several weeks it had been common knowledge that he was fighting a losing battle and that there was no hope of his recovery.

It is very difficult to convey how marked was his influence generally in the well-being of the community in which he worked. Here, however, is a brief outline of what he accomplished. Born at Geelong, his boyhood was spent in Victoria, and at the outbreak of the last war he was a medical student at Melbourne. Enlisting at once, he left

with the Third Light Horse Field Ambulance as a stretcher bearer. It is easy to picture him as a young man of outstanding physique and courage sharing for the long months the unending toil of carrying wounded down the narrow saps and gullies at Anzac. It should be remembered too that at that time there was no carrying on the shoulders in squads of four; each stretcher was the task of two men and the strain on arms and body was very great. I have heard him describe, as the climax, conditions during the August fighting on the left towards Suvla. In full midsummer with greatly depleted numbers and worn out after months of poor feeding and sickness, it fell to a few stalwarts to get out hundreds of wounded. In the heat and under such conditions it was a physical impossibility to do so, and the story will not bear retelling. It is not too much to say that the work of these months, with its unending strain, took from Shugg much of the reserve strength that would have meant a longer life, while at the same time it gave him much of his remarkable understanding of his brother man. Early in 1916 medical students were returned to finish their courses, and Shugg duly graduated with honours in 1918. An appointment to the Tasmanian Hydro-electric Commission gave him his first contact with this State when he was allotted as medical officer to the large works then under construction at the Great Lake. Before finally settling in Tasmania, he held a position as resident at the Children's Hospital, Melbourne. Some years of practice at New Norfolk preceded his commencing in Hobart.

Although his primary interest was in paediatrics, he soon built up a large general practice, and during the next seventeen years became more and more to be looked on as an authority on children and their problems. A long association with the Mothercraft Home and his appointment as honorary physician to the children's wards at the Royal Hobart Hospital, made it inevitable that he should be turned to at once on the outbreak of the severe epidemic of anterior poliomyelitis of 1930. He was selected as a member of the advisory council set up to cope with the epidemic and later appointed to take charge of the cases which were centralized at the Royal Hobart Hospital. Logical and far-seeing, he planned from the beginning that these cases should remain under close supervision until all possible recovery had been effected. Simultaneously a census of all victims of previous epidemics and of all crippled children in the State was undertaken as a forerunner to the systematic working of the newly formed Tasmanian Society for the Care of Crippled Children. President of this society for two years, he was for the remainder of his life its principal inspiration. The culminating point of the society's work was the effort by which funds were made available for the building of "Wingfield House", where the children are treated and from where in many cases they are discharged fit to live a normal life again. His principal other interest was perhaps the welfare of the returned men. His service to them consisted of much committee work as well as the presidency of the Tasmanian branch of the Returned Sailors and Soldiers' Imperial League of Australia and a trusteeship of Gellibrand House.

As a medical man he was one of the most valued members of the Association. Only last year he was President of the Tasmanian Branch, and for a number of years he had been one of the two Branch representatives on the Federal Council. He wrote little, but gave much good clinical material to our monthly meetings. In council he was wise and broad-minded, and never more so than when contentious

matters arose, as in the medico-political activities of the last few years. On these occasions he did much to find a basis on which opposing views might agree. All these activities, with a large practice, told on a constitution never really inherently strong. For some years we had known he should do less, and it was hoped that with help in his practice he would be able to manage. The onset of the war, however, meant much additional work for him on boards and at the Military Hospital, and some three months ago it became clear that his strength was no longer equal to the task. After a few weeks in hospital the end came. It was a great source of happiness at this time to know that his work had been recognized in the last honours list. His Excellency Sir Ernest Clark visited Stowell Hospital and invested Dr. Shugg with the insignia of a Commander of the Most Excellent Order of the British Empire in the presence of his wife and family, and this gracious action was deeply appreciated by the community.

So much for his life's work; what shall I say of the man himself? Of marked dignity of person, he was essentially

a merry soul and greatly liked. He brought to his work keen observation, much experience, and read widely, and so achieved great results. As his patient I remember the strength and comfort he brought with him, and as a consultant, as in a difficult obstetric case, he brought the same qualities and more. I know of no other medical man who, coming as a stranger, became so essentially one of us. This I feel was due to his ideally happy marriage, the environment of his old colonial home, "Wingfield", and his family. In these last months his courage was exemplary, and he leaves a great tradition to his sons and his profession.

Sir John Gellibrand, in a letter to myself, writes: "It was indeed a grief to hear of Shugg's death—a man we could ill afford to lose, even if Australia was better off than she is in good men."

Dr. W. W. Giblin writes: The death of Dr. A. W. Shugg is an irreparable loss to his many friends, but most of all to the crippled children of Hobart. His special knowledge of their treatment, combined with his happy knack of gaining their confidence, cannot be replaced. Not only has he carried the

burden of a busy practice, but also found time for extensive community service in spite of the fact that he knew he was suffering from an incurable ailment. He never allowed this knowledge to daunt his courage or lessen his sense of humour, so that few of his friends realized the gravity of his condition.

YAKOFF GORR.

We regret to announce the death of Dr. Yakoff Gorr, which occurred on August 20, 1941, at Shepparton, Victoria.

SAMUEL MIDDLETON WARE.

We regret to announce the death of Dr. Samuel Middleton Ware, which occurred on August 21, 1941, at Taree, New South Wales.



Naval, Military and Air Force.

LECTURES ON ARMY MEDICINE AT ADELAIDE.

THE Deputy Director of Medical Services of the Fourth Military District announces the following programme of lectures on army medicine for September, 1941.

1. The lectures and demonstrations will be given at the Institute of Medical and Veterinary Science, Frome Road, Adelaide, on Sundays, mornings and afternoons, September 14 and 28.

2. The lectures are open to officers of active and reserve lists, Australian Army Medical Corps, Fourth Military District, members of the Australian Army Nursing Service, and senior non-commissioned officers of Australian Army Medical Corps units.

3. Medical officers of the Royal Australian Navy and the Royal Australian Air Force are invited.

4. Medical practitioners and medical students are invited.

Sunday, September 14, 1941.

10 a.m. to 12.30 p.m.—

(1) Lieutenant-Colonel E. A. H. Russell: "The Medical Organization of A.R.P. in South Australia".

(2) Squadron Leader W. B. Stephens: "Principles of Aviation Medicine".

(3) Lieutenant-Colonel J. R. Kearnan: "Organization of a District Headquarters—the Staffs and Services".

2 p.m. to 4 p.m.—

Symposium: "Some Tropical Diseases"—(1) Professor Harvey Johnston: "Parasitology"; (2) Dr. J. E. Bateman: "Clinical Aspects".

Sunday, September 28, 1941.

All-day tactical exercise and instruction in map reading. Further particulars will be issued for Australian Army Medical Corps officers.

Australian Medical Board Proceedings.

VICTORIA.

THE following statement has been received for publication from the President of the Medical Board of Victoria.

The Medical Board of Victoria, on Thursday, July 31, 1941, having held a full inquiry into certain allegations of infamous conduct in a professional respect against No. 4622, Francis Timothy Hartnett, a person registered in the medical register of Victoria, finds him guilty of the following acts or omissions:

That, on the 20th day of March 1939, while acting as Clinical Assistant to Out Patients Surgeon at Royal Melbourne Hospital, the said Francis Timothy Hartnett did request and induce one Ralph Gordon Dominey of 23 Fernanagh Road, Camberwell, in the State of Victoria, an Out Patient of the said Hospital, to receive treatment from the said Francis Timothy Hartnett in his capacity as a private Medical Practitioner at his surgery in Burwood Road, Camberwell, with the intent that he should derive financial benefit from such treatment.

That, during the month of February, 1939, while acting as Clinical Assistant to Out Patients Surgeon at Royal Melbourne Hospital, the said Francis Timothy Hartnett did request and induce one George Robert Cook, of 185 Nicholson Street, Coburg, in the State of Victoria, an Out Patient of the said Hospital, to receive treatment from the said Francis Timothy Hartnett in his capacity as a private Medical Practitioner at his surgery in Burwood Road, Camberwell, aforesaid with the intent that he should derive financial benefit from such treatment.

That, on the 22nd day of May, 1939, while acting as Clinical Assistant to Out Patients Surgeon at Royal Melbourne Hospital, the said Francis Timothy Hartnett did request and induce one Daniel Ellaway, of 16 Russell Street, Northcote, in the State of Victoria, an Out Patient of the said Hospital, to receive treatment from the said Francis Timothy Hartnett in his capacity as a private Medical Practitioner at his surgery in Burwood Road, Camberwell, aforesaid with the intent that he should derive financial benefit from such treatment.

The Board is satisfied that the said Francis Timothy Hartnett is guilty of infamous conduct in a professional respect within the meaning of sub-sections (1) and (6) of

Section 7 of the *Medical Act 1928* as re-enacted by Section 4 of the *Medical Act 1933* and orders that the name of the said Francis Timothy Hartnett be erased from the medical register of Victoria at the hour of five o'clock in the afternoon of the eighteenth day of August, 1941.

The Medical Board has recently been investigating cases where medical certificates of an untrue or misleading character have been issued by certain medical practitioners and, in this connexion, it is pointed out that a medical practitioner who gives such a certificate lays himself open to a charge of infamous conduct in a professional respect, which may result in the erasure of his name from the medical register.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Barnes, Winstanley, M.B., B.S., 1935 (Univ. Sydney), 10, Victoria Street, Mayfield.

Grace, Stanley St. John Starkey, M.B., B.S., 1939 (Univ. Sydney), 70, Shell Cove Road, Neutral Bay.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phoenix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

Editorial Notices.

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